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# The Impact of Canadian Direct-to-Consumer Prescription Medicine Advertising on Prescription Volume

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A Thesis

in the

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## ABSTRACT

The Impact of Canadian Direct-to-Consumer Prescription Medicine Advertising on Prescription Volume

Kristian A. Stubbs

Canadian pharmaceutical companies are increasingly using direct-to-consumer advertising (DTCA) of prescription medications in an attempt to stimulate sales. While published literature on the impact of DTCA is limited, one study conducted in the United States by Basara (1996) suggested that DTCA has a positive impact on new prescription volume and thus sales. This study investigates the reliability of findings of Basara (1996) and extends them using a Canadian prescription medication that was advertised directly to consumers.

IMS Health Canada new prescription data was obtained for a prescription medication. The same promotional-response modeling technique known as intervention time-series analysis that Basara (1996) used, was used to investigate the potential for DTCA to impact new prescription volume for this medication. Results suggest that DTCA did not have an identifiable impact on new prescription volume for this product. Findings suggest that caution should be used when interpreting Basara's (1996) findings in the Canadian context. Specifically, the impact of DTCA appears to be dependent on product, market, and advertisement related factors. Research implications, limitations, and directions for future research are discussed.

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# CHAPTER 1

# INTRODUCTION

This research thesis includes a review and critical synthesis of literature relevant to promotional response modeling and pharmaceutical direct-to-consumer advertising (DTCA). Through an empirical investigation of the impact of direct-to-consumer advertising of a prescription medication in Canada, this research contributes to the overall knowledge of promotional response modeling in a new and under-studied market. In addition, this research presents insight into the impact of DTCA of prescription medications worthy of consideration by academics, industry professionals, and other key stakeholders.

The relationship between sales and promotion has been extensively investigated over the course of the last 40 years. Findings suggest that promotion, whether focused on price or advertising, does in fact have a significant impact on sales volumes. While researchers in the area have focused attention on determining the optimal method for measuring the magnitude, duration, and mechanism of such an impact, there remains much to be learned as far as the instance and dynamics of such an impact in different market environments.

Direct-to-consumer advertising (DTCA) of prescription medications is a relatively new concept within the pharmaceutical industry. Cutrer and Pleil (1991) define DTCA as any promotional effort by a pharmaceutical company to present prescription drug, or drug therapy information to the general public through the lay media. Traditionally

pharmaceutical marketers have invested the large majority of advertising resources in professional focused advertisements appearing mainly in medical journals. This focused approach emerged in part due to the fact that the use of prescription products may only occur with the endorsement of a licensed physician. Another contributing factor to this focused approach has been the regulatory environment that, in many countries, prohibits the advertisement of prescription medications to consumers or patients. With increased regulatory freedom, and broadening interpretations of regulations, pharmaceutical marketers have increased the use of DTCA in recent past.

Research in the United-States investigating DTCA has revealed that the majority of advertising (63%) is for medications promising to ameliorate symptoms, while 26% and 11% were for the treatment or prevention of disease respectively. Promotional appeals used in these advertisements include emotional appeals (67%) and encouragement of consumers to consider medical causes for their experiences (39%). The factual content of advertising varied considerably and benefits were often described with vague, qualitative terms (Woloshin et al, 2001).

Advertisement content variability is furthered by pharmaceutical marketer's efforts to ensure that advertisements are within regulatory guidelines. These guidelines vary considerably from country to country, and the content of such guidelines is often outdated and open to interpretation.

Empirical research investigating the impact of DTCA is limited and consists of relatively few studies using differing methodologies. One of the elements confusing the study of the impact of DTCA is the need to define the dependent variable impacted by advertising efforts. This impact could be observed at any of the 5 intervals in the buying decision process (Lee, Johnson, 1999):

1. Need Recognition
2. Information Search
3. Alternative Evaluation
4. Purchase
5. Post-purchase Evaluation

The most important or desirable outcome associated directly or indirectly with advertising is the purchase or use of an advertised product. One study conducted in the United States investigated the impact of DTCA on new prescription volume of a prescription medication. This research found that DTCA was effective in generating new prescriptions while the campaign was in effect, with residual but declining effects after discontinuation (Basara, 1996).

The emphasis on using DTCA to promote newer medications raises safety issues. There is a concern about pushing very rapid, widespread use of new drugs before enough is known about their long-term risks. In the United States there have seen three products advertised to the public that were later withdrawn for safety reasons. Baycol, which is a

cholesterol lowering drug, Rezulin for diabetes, and Prepulsid for night-time heartburn (Health Matters, 2002).

This research thesis attempts to build on Basara's (1996) research by replicating her findings, and to extend them into the Canadian market. In addition this research was designed to explore the potential for regional differences in the degree of impact. This is an important element considering regional and cultural differences in the Canadian market (Rotenberg, 1983).

Findings compliment existing literature on promotional response and the subject of DTCA. Furthermore, this research represents the first to quantitatively investigate the impact of Canadian DTCA. It provides a good starting point for future research focusing on the impact of DTCA on sales volumes of prescription medications in Canada, and provides important information to marketing practitioners working in the field of pharmaceutical marketing. Finally, this research makes use of a methodology that is receiving attention by market researchers attempting to measure the impact of specific events, namely interrupted time-series analysis.

This report consists of 5 chapters. Included in this study are a detailed literature review, research hypotheses, methodology, analyses & results, and a discussion including implications and recommendations for future research.

# CHAPTER 2

# LITERATURE REVIEW

## 2.1 Promotional-Response Modeling

The relationship between sales and promotion has been investigated extensively over the course of the last 40 years. Palda (1964) published one of the first studies of the relationship between sales and advertising. The suggestion that promotion could have an impact on sales volumes raised the question as to the duration of such an impact. In a review of the relevant literature concerning cumulative advertising effects and their duration Clarke (1976) concluded that the impact of advertising on sales volumes lasts for months, rather than years. Conclusions by Palda (1964) and Clarke (1976) set the stage for future research investigating the existence, magnitude, and duration of the impact of promotion on sales volume.

It is important to recognize that in the measurement of promotional-response, promotion has been defined in a variety of ways. While promotion in theory can involve any one of the variables in the marketing mix (e.g. sales-effort), promotional elements the most frequently studied are price and advertising, while products studied are generally consumer goods (Gupta, 1988). While price manipulation represents a very interesting area, the focus of this research is advertising.

The concept of promotional response modeling represents a field of interest both from a scientific and a practical perspective. Leone and Randall (1980) found that variability in results due to specification problems such as multicollinearity, aggregation bias, failure to consider the simultaneous nature of sales and advertising, or failure to account for serial correlation has and continues to be a problem. They suggested that in order to overcome these problems, and create models suitable for generalization there is a need for replication. In this pursuit most studies that have tried to estimate the effects of advertising on brand sales using field data have focused on the many technical issues involved in efficiently capturing the unbiased effects of advertising given the limitations of field data. While some studies have uncovered some significant effects of advertising these effects can be fragile and dependent on certain conditions (Tellis, Chandy, and Thaivanich, 2000). Aaker and Carmen (1982) suggested that more studies are needed for relatively new products, in locations other than the U.S. and Europe, and for products other than packaged goods.

Generally, published literature on the subject of promotional-response modeling suggests that there does exist a relationship between sales and advertising expenditure. Continued research on sales response and promotion including meta-analyses has confirmed that the effects of advertising are significantly greater than zero but vary by market and product characteristics (Assmus, Farley, and Lehman, 1984).

With further evidence of the relationship between sales and promotion some researchers have begun to focus on the consumer. Specifically, the question of promotional response

and consumer variability has been addressed in the literature. Deighton (1984) concluded that beliefs about products are determined by an interaction between advertising and objective evidence about product performance. More specifically, advertising has an impact on product evaluation when coupled with objective evidence. If an advertiser makes a claim and the consumer discovers through product testing that the claim is valid, the consumer may not really care whether other products also satisfy that claim (Hoch and Ha, 1986). Behavioural theory and laboratory studies indicate that response to advertising exposure is nonlinear and stronger among subjects familiar with the brand or message (Tellis, 1988).

While the investigation into consumer related factors continues, the fundamental question of how marketing mix variables affect consumers purchase decisions and thus the sales of a brand remains. Interest in this area is growing with increasing competition in many areas, escalation in promotional expenditures, and the growing number of communication mediums available (e.g. internet, e-mail, wireless tools). Though research has shown that price and sales promotions have a significant impact on consumers' brand choice purchase time, and purchase quantity, the question of whether the increase in sales is due to switching, borrowing, or stock-piling is one of interest to both marketing researchers and practitioners (Gupta, 1988). Tellis (1988) concluded that advertising appears effective in increasing the volume purchased by loyal buyers but less effective at winning new buyers. For loyal buyers, high levels of exposure per week may be unproductive because of leveling off of advertisement effectiveness. Brand switching effects can result from advertising building brand awareness or altering beliefs about brands. Repeat

purchasing effects can result from these same direct effects of advertising, or alternatively, from an interaction between advertising and brand usage whereby advertising serves to illuminate the brand usage experience (framing-effect) Furthermore, advertising's effects can be negated by the consumer's personal experience in using the product (Deighton, Henderson, and Neslin, 1994). Given the effectiveness of the other marketing variables, especially in brand switching, a reasonable strategy would be to promote trial with displays, features, and coupons and then motivate repurchase and more intensive purchases with advertising (Tellis, 1988), (Mela, Gupta, and Lehmann, 1997).

Advertising is generally thought to have a current-period influence on sales, called the current effect, and a long-term influence beyond the current-period influence on sales, called the long-term or carryover effect. Researchers have used sales-response and choice modeling economic models to estimate both of these effects of advertising (Tellis and Weiss, 1995). It is useful to define the time-period within which an impact is measured. The effects of marketing on consumers' choice behaviours can be considered in terms of short-term (e.g. weekly), medium-term (13-weeks or quarter), and long-term (years) (Mela, Gupta, and Lehmann, 1997).

Despite extensive research on advertising, managers and public policy makers face considerable uncertainty about its role in contemporary markets (Tellis, 1988). There exists a clear need to replicate and extend the findings of past promotional-response research into new markets in order to enhance the overall understanding of this area of

marketing. Continued investigation will help to broaden past findings and provide input into conclusions that can be generalized and formalized into marketing theory.

## 2.2 Promotional Response Modeling in the Pharmaceutical Industry

It is of interest to note that one of the first published studies of the relationship between sales and advertising was conducted using data comparing sales and advertising of a medicine between 1907 and 1960 (Palda, 1964). Since that time, the relationship between sales and promotion has been studied extensively. The majority of research in this field has focused on consumer goods, due in part to the wide spread use of advertising of these products, and the availability of data for analysis. One market that is receiving increasing attention is that of the pharmaceutical industry. Due mainly to the relative novelty of advertising to consumers in this industry, a number of studies have addressed the impact of DTCA. While most research in this area has focused on the impact on consumers, some research has addressed the impact of DTCA on pharmaceutical manufacturers, physicians, and the public-at-large.

Prescription medications are not like consumer products. Prescription medications are available only with a prescription; are selected by physicians, managed care organizations, and hospital formulary committees; and are purchased only through a pharmacist in a licensed pharmacy. This raises the question of why to consider direct-to-consumer advertising, if consumers are not able to make the final purchase decision of any given medication. Basara (1994) proposed several reasons for the increase including,

increasing ability of consumers to influence physicians, the use of advertising to manage safety concerns and educate consumers, the use of advertising to influence physicians through the repetition of key marketing messages, and the use of advertising as a differentiation strategy.

In their review of the research on the subject, Eichner and Maronick (2001) found that consumers are increasingly aware of DTCA, and are often times requesting medications seen in advertisements. This kind of activity has raised some concern amongst physicians who want to ensure that consumers are provided with a fair-balance of benefit versus risk information.

Those in favour of DTCA cite the benefits to consumers and the pharmaceutical industry. For consumers' benefits arise when advertising achieves its theoretical goal of providing information. This could result in a more knowledgeable patient who may have learned about preventative health care measures, alternative therapies, methods for proper use of medications, or even how to better choose providers of health care (Perri, and Dickson, 1987).

Educating patients about medicines is becoming more important to pharmaceutical marketers. This new focus has occurred for several reasons related to the overall increased education of patients. Specifically, educated patients are more compliant with therapy recommendations than uneducated patients. They are more willing to discuss symptoms, adverse effects, and quality of life concerns with health care professionals, as

well as to question therapy recommendations. These patients refill prescriptions and follow dosing instructions (Basara, 1994).

Although it is an obvious goal of advertising, generation of demand is not always simple. There are two types of demand: primary and selective. Primary demand is demand for a product category, while selective demand is demand for a specific brand name product. Creating such demand is a complex process of influencing consumers' attitudes, beliefs, and purchase intentions by establishing unfulfilled needs or wants (Basara, 1994). Ultimately, effective advertising strategies increase product purchases. By making consumers aware of a product and communicating its benefits, advertisements encourage product selection and increase sales revenue.

Pharmaceutical manufacturers are faced with significant obstacles to effectively generating both selective and primary demand in the Canadian marketplace. Specifically, due to the regulations governing DTCA in Canada advertisers are generally not able to effectively communicate the association between product benefits and intended use. Complicating this are high levels of competition in several different markets making truly unique products uncommon.

While much of the past research has been focused on consumer awareness of and reaction to DTCA, the fundamental question of whether or not such advertising has an impact on prescription volume for a given advertised product needs to be addressed. While some quantitative research has been published on the subject (Basara, 1994), (Eichner,

Maronick, 2001), results and methodologies are not consistent. Furthermore, at the time of this research, and to my knowledge, there are no known investigations of the impact of DTCA on prescribing volume in Canada.

## 2.3 Replication of Promotional-Response Modeling Research

In 1996 Basara published results of a time-series analysis of new prescription data for a migraine product. This research suggested that advertising of prescription medications directly to consumers could result in significant increases in new prescription volume for the advertised product. This finding was not fully supported by findings of Eichner and Maronick (2001), which suggested that in terms of the impact of DTCA on sales of specific drugs, the data show that expenditures do not always correlate with market share within a category.

Basara's (1996) finding that DTCA does in fact have an impact on prescription medication volume is interesting and warrants further attention. While this finding is important from a promotional-response modeling perspective, it is also has significant implications for key stakeholders in the pharmaceutical industry. More specifically, the potential for DTCA to increase sales is an important consideration for pharmaceutical manufacturers considering future investment in this area, and government and private payers considering the potential cost of such initiatives in terms of increased medication usage. In addition, physicians and consumer groups are especially interested in this area due to the potential changes in patient/consumer behaviour.

To put the Basara (1996) research into perspective it is important to understand the parameters of this research. Specifically, the selection of an appropriate DTCA campaign was an important consideration in the planning and execution of the research. Specifically, there was a concern that a campaign be selected that minimized the effect of mitigating circumstances or lack of data. Table 2.1 includes a list of criteria used to minimize the effect of mitigating circumstances:

**Table 2.1: DTCA Campaign and Prescription Medication Criteria for Application of Time-Series Analysis**

| |
|---|
| **To ensure accurate time-series analysis, the DTCA campaign should:** |
| -Have begun after January 1993 |
| -Have been the first DTCA effort made for the product |
| -Include product-specific print and/or television copy |
| |
| **The prescription medication advertised directly to consumers should:** |
| -Have been on the market as a prescription medication for at least 6 months before the DTCA campaign began |
| -Have relatively few approved indications |
| -Have no over-the-counter competitors |
| -Have no prescription medication competitors that were concurrently or previously advertised directly to consumers |
| -Treat a condition that is not related to cosmetic or lifestyle concerns |
| -Treat a condition that is relatively common among the U.S. population |

The rationale behind some of Basara's (1996) criteria is obvious and driven by the inherent characteristics of time-series analysis (e.g. historical data). However, the criteria regarding the prescription medications applicable to this type of analysis are restrictive considering the competitive nature of the pharmaceutical market.

A deviation from the proposed criteria, Basara (1996) selected a product (Imitrex) used for the acute treatment of classic migraine headaches. This product was the newest

therapy available in a category consisting of old, unpromoted, and relatively ineffective products.

Basara's product selection is significant in this research due to the fact that it did not meet the criteria suggested in the study. Specifically, Imitrex DTCA did not include product-specific print or television copy; rather advertising was considered informational and focused on the treatment of migraine generally. Moreover, while Imitrex did not have any prescription competitors that had used DTCA in the past, it did have some competition in the form of over-the-counter medications such as acetaminophen, which is often used by migraine sufferers. Another interesting factor related to the use of Imitrex as a product for analysis is the nature of the market in which it was competing. More specifically, this market was not active from a marketing perspective prior to the product launch and subsequent DTCA campaign. This kind of market is relatively rare considering the large investment in pharmacological treatments for conditions as common as migraine headache. As well considering the substantial impact of migraine headaches on sufferers' quality-of-life (e.g. pain, loss of productivity, social inconvenience) this market is likely composed of patients eager to locate solutions to a serious health related problem.

Basara's (1996) research indicated a significant impact of DTCA on prescription volume, and was the first retrospective assessment of the value of DTCA in the U.S. pharmaceutical market. This is an important finding, and one that merits replication and extension in different markets outside of the United States, and using different products.

The value of such replication will be to assist in the measurement of the reliability of Basara's findings. Furthermore, extension of this research to examples that better reflect the reality of today's pharmaceutical market including increased competition, blockbuster products (i.e. high market share and sales volume), and international markets, will increase the usefulness of Basara's findings to key stakeholders.

There is clear a need in the pharmaceutical market generally, and in the Canadian pharmaceutical market specifically, for continued investigation of the impact of DTCA on prescription volumes. Future research in this area offers the contribution of extending findings of both Basara (1996) and Maronick and Eichner (2001), and extending knowledge of promotional-response modeling in new and unique markets

## 2.4 The Canadian Pharmaceutical Market

Pharmaceuticals are one of the largest and fastest growing retail markets within Canada. In fact the total Canadian pharmaceutical market produced $9.5 billion in drug store and hospital sales in the year 2000 increasing at +14.6% over 1999 (IMS Health Canada Inc, 2001). Sales in Canada compare to the United States which produced $140.0 billion in sales in the year 2000, increasing at +14.9% (IMS Health America Inc, 2001). In Canada there were approximately 285 million prescriptions filled in 2000 increasing at 7.7% over 1999 levels (IMS Health Canada Inc, 2001).

Due to its large size and growth Figures the pharmaceutical market is receiving increasing attention from pharmaceutical manufacturers, government and private payers, the medical

community, and consumer groups. While pharmaceutical manufacturers have a vested interest in profitability, other stakeholders are concerned with issues such as increased demand for pharmaceutical products leading to rising costs.

Of particular concern is the fact that sales growth is higher than prescription growth in both Canada and in the United States. This suggests that other factors are influencing growth levels. These factors may include changes in healthcare policy; price increases, new products and technologies; new disease states or treatment options; and a change in the healthcare needs of the general population. Each of these factors is important to understand in order to put the potential for investment in promotional activities to increase sales volumes into perspective.

## 2.5 Pharmaceutical Promotion

Drug promotion can be defined as all informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs (World Health Organization, 1999). By definition the aim of promotion is to stimulate product sales.

Up until the early 1980's the pharmaceutical industry focused advertising efforts solely on healthcare professionals. Such promotion typically included healthcare related journal advertising, product sampling, and selling activities. With increased competition, the introduction of several new products, and the growing over-the-counter (OTC) market,

pharmaceutical manufacturers have begun to look at new and innovative ways of marketing their prescription medicines. Approximately 20 years ago, the pharmaceutical industry began marketing prescription drugs directly to consumers. The Food and Drug Administration (FDA) imposed a moratorium on this marketing strategy in 1983, then lifted it in 1985 (Center for Drug Evaluation and Research, 1985).

Research suggests that increased competition, generic substitutes, and government calls for restraint in healthcare, have caused pharmaceutical manufacturers to switch to a more consumer-oriented stance and have turned to advertising directly to the end user (Maddox and Katsanis, 1997).

Canada has not followed the U.S. example. While Health Canada acknowledges that consumer demand for information is increasing, and that industry and patient support groups would like to provide this information, it cites concerns about DTCA, relating to the ability of the consumer to interpret this type of information and the impact on physician prescribing practices, the potential for increased healthcare costs, and mounting evidence that inappropriate prescription drug use is increasing. However, a 1978 amendment, designed to allow pharmacists to post comparative prices, allows DTCA as long as the person shall not make any representation other than with respect to the brand name, proper name, price and quantity of the drug. As such, ads that describe a medical condition and then direct consumers to a doctor, telephone number or Web site are legal Advertisements that mention the brand name of the drug but do not say what condition it

treats are also considered legal. Legal issues arise when mentioning the brand name and the therapeutic use of a drug in the same advertisement (Silversides, 2001).

While there are clear differences between the policies relating to DTCA in the U.S. and Canada, the issue of spillover between markets increases the relevance of the potential for DTCA to impact prescription volume in Canada. Currently it is estimated that spillover of U.S. media advertising in Canada is significant. Specifically, in 1998 English-Canadians estimated that they spent 50 per cent of their time watching American television channels (CROP, 1998). Considering the $2.5 billion spent on DTCA in the U.S. during 2000 (Rosenthall et al., 2002) it is highly likely that a large number of Canadians are exposed to U.S. based pharmaceutical DTCA in one form or another.

However, due to differences between the Canadian and American healthcare systems, and markets generally, one must exercise caution when extending conclusions derived from market research conducted in the U.S. to Canada. Some important differences include the differences in insurance, product availability, product prices, and product branding.

## 2.6 Key Parties Affected by DTCA

There are several key parties affected by the potential for DTCA to increase sales of pharmaceutical products. While pharmaceutical manufacturers are concerned with the sales, other parties are concerned with the potential for increases in inappropriate product demand and related costs.

Available literature suggests that one of the major concerns is the potential for consumers to pressure physicians into prescribing inappropriately (Masson & Rubin, 1985; Krieger, 1983). Another concern is that DTCA may serve to increase drug prices, since these ads will supplement and not replace present advertising (Krieger, 1983; Kopp, 1996). Other concerns suggest that such advertising may serve to confuse consumers by inadequately communicating risk information and other treatment options. Finally, opponents fear that DTCA may lead to excessive demands on the health system (Smith, 1999).

From another perspective DTCA may prove beneficial and a way to meet the growing demand for medical information, empowering consumers by educating them about health conditions and available treatments.

It is useful to examine each of the parties potentially affected by the impact of DTCA on medication sales volumes in order to the importance of this issue into context.

### 2.6.1 DTCA and the Canadian Government

Given the high growth in DTCA Health Canada is carefully considering whether or not pharmaceutical companies should be allowed to advertise medications directly to the general public (Wysong, 1999). While the impact of DTCA has long been an issue of debate within Canadian government the lack of published research has forced this debate to be based on theoretical assumptions and comparisons to the U.S. market.

Canada has relatively little experience with DTCA when compared to the United States. While there are few instances of DTCA of prescription medications taking place in Canada, there has been much debate surrounding its potential to be used.

There is need for the Canadian government to enhance its understanding of the potential outcomes associated with DTCA of prescription medications, specifically, the question of whether or not DTCA will increase prescriptions. This is particularly important from a cost or sales perspective so that future healthcare related expenditures can be planned for accordingly.

### 2.6.2 DTCA and Canadian Pharmaceutical Manufacturers

One of the primary concerns for pharmaceutical manufacturers is profitability. While DTCA is undoubtedly used in an effort to stimulate sales, some companies suggest that there are several positive outcomes potentially associated with its use. Specifically, Canada's Rx&D which is an association representing a large number of Canada's trade-name pharmaceutical companies suggests that DTCA can provide valuable information to consumers and encourage Canadians to learn more about prescription medicines. The Rx&D supports a regulated approach to pharmaceutical advertising and has proposed that advertising can raise awareness of effective new therapies and improve the overall health of Canadians by helping Canadians recognize early symptoms and informing them about potential treatment options (Globe and Mail, 2001).

Canadian pharmaceutical manufacturers have an interest in better understanding DTCA. Specifically, from a profitability perspective whether or not DTCA has a positive impact on sales volumes. As well, an understanding of the impact of the impact of existing examples of DTCA on prescription volumes will help determine whether or not these initiatives are increasing awareness of disease symptoms and treatment options. This better understanding will aid in the debate over whether or not to allow DTCA in Canada, and will help in the determination of when, where, and how much to invest in DTCA.

### 2.6.3 DTCA and Private-Payers

Private-payers or insurers are responsible for the reimbursement of the costs associated with prescription medications. Private-payers must estimate the demand for any given medication based on a variety of factors including, historical data, and other external factors. This data is then projected into future cost estimates based on the prevailing prices of medications currently available. The introduction of another factor potentially impacting demand such as DTCA has the potential to increase demand and thus costs. Compounding this effect is the fact that the vast majority of medication promotion, including DTCA is for patented products, which are generally more expensive than generic or multi-source products.

The number one concern for private-payers covering the cost of healthcare is the potential for increases in expenses associated with DTCA (Globe and Mail, 2001). As such, these

entities are in need of insight in terms of the potential impact of DTCA on prescription volumes for medications being advertised.

### 2.6.4 DTCA and the Patient

The typical Canadian patient has had little if any exposure to pharmaceutical companies operating in Canada or the products they manufacture and sell. This is due largely to regulations strictly forbidding such marketing practices as advertising, sampling, and direct selling to these individuals. As such, patients have the potential to be significantly effected by a sudden increase in marketing communications being directly aimed towards them.

Consumers or patients in this case, are complex, each possessing different levels of education, information, and knowledge. It is reasonable to expect that some consumers may find themselves more easily persuaded by marketing efforts. Research has demonstrated that the medical condition of a consumer has a significant impact on attitudes towards advertisements relating to said conditions and/or treatments for such conditions (Perri & Dickson, 1987). Furthermore, the age and medical knowledge of the consumer has a greater influence on preferences for information on drug and treatment alternatives (Doucette, and Schommer, 1998). While there may be some variability in response, there exists an opportunity for both consumers and marketers to benefit from increased information sharing.

The notion of creating a balanced means of communication between both pharmaceutical manufacturers and consumers has arisen in published literature. More specifically, consumer groups have expressed concern that DTCA meet certain criteria with respect to balancing safety and efficacy statements with statements regarding risk and limitations of efficacy. Furthermore, recommendations have been made that consumers have access to approved labeling of products, as well as reassurance of complete privacy when accessing such information (Golodner, 1997).

The question arises as to what consumers will do with information regarding prescription medications. Maddox and Katsanis (1997) found that while patients are quite comfortable discussing a prescription drug that is advertised, those exposed to DTCA may be less likely to initiate discussion and are unsure whether or not they will seek additional information (Maddox, and Katsanis, 1997).

The potential impact of DTCA on Canadian consumers or patients is significant. As these end-users are increasingly encouraged to take part in their own healthcare the potential for product misuse, or inappropriate consulting or non-consulting become issues. As such, there is an important need to better understand the potential for, and likelihood of pharmaceutical DTCA to influence these individuals so that appropriate regulations may be set, and DTCA content designed appropriately. One of the first steps necessary to developing this understanding is the identification of whether or not pharmaceutical DTCA does in fact influence prescription volumes for products being advertised.

### 2.6.5 DTCA and The Medical Community

The medical community has long been the focus of attention of the majority of pharmaceutical manufacturers marketing initiatives. As a result, many have had the opportunity to experience both positive outcomes and negative consequences related to pharmaceutical marketing. While positive outcomes often revolve around the sharing of important information, negative consequences often involve misleading promotional messaging leading to misuse of prescription products.

Published research with physicians suggests that DTCA of prescription drugs is expected to produce negative outcomes for both themselves and consumers including increased demand for advertised drugs, negative effects on the patient-physician relationship, and increased patient questioning of the prescribing decisions (Cutrer and Pleil, 1991) Heesels (1993) found that Canadian physicians were skeptical as to the potential for positive outcomes associated with increased use of DTCA.

Some evidence however suggests that physicians' attitudes towards DTCA may be changing. In 1998 the American Medical Association (AMA) endorsed DTCA of prescription drugs, provided the AMA has a standard-setting role with the FDA in determining its content (Eichner and Maronick, 2001).

The potential impact of DTCA on the Canadian medical community is significant. As these individuals are ultimately responsible for the appropriate dispensing and use of

prescription medications, an increase in inappropriate patient demand could have serious implications. There is a need to better understand the potential for, and likelihood that DTCA of prescription medications will increasing prescribing so the medical community may prepare itself appropriately to deal with increased demand for information and specific products.

## 2.7 The Impact of DTCA

The impact of pharmaceutical DTCA is difficult to measure due to the variety of ways in which an impact can occur. More specifically, DTCA can raise awareness, familiarity, information seeking, prescription request, and actual prescription filling. In a literature review of prior research on the subject of DTCA it was found that several authors have investigated the issue of DTCA and its impact on the marketplace (Eichner and Maronick, 2001). Published research on the subject is often either government of industry sponsored, and methodologies used are often inconsistent and conclusions drawn tend to be difficult to interpret.

One clear conclusion of research emanating from the U.S. is that consumers, after over 20 years of DTCA, are aware and increasingly familiar with this form of pharmaceutical promotion (Smith, 1991). However, relatively few consumers exposed to DTCA actually request additional information from their physician (Wilkes, Bell, Kravitz, 2000), (Center for Drug Evaluation and Research, 2000). Common reasons for not speaking with physicians include fear of damaging the doctor-patient relationship (Alperstein and Peirot,

1993), or miscomprehension of the advertising message (Morris et al., 1986). These problems may be attributable or compounded by imperfect information in DTCA (Viscusi et al., 1986), (Tanouye, 1998).

Roth (1996) found that people are more likely to engage in preventive health behaviours when they become aware of a condition and perceive themselves to be susceptible to that condition. This tendency is the source of concern as physicians find themselves increasingly asked to discuss conditions and prescribe medications advertised to patients (Ukens, 1992), (Schwartz, Soumerai, and Avorn, 1989).

In an effort to assess the impact of DTCA originating in Canada and the U.S. Health Canada commissioned research to study how advertising influences what doctors prescribe. The study was designed to examine the relation between DTCA and patient requests for prescriptions, and the relationship between patient requests and prescribing decisions. Results of the study suggested that patients requested prescriptions for products in 12% of surveyed visits. Of these requests, 42% were for products advertised to consumers. The research concluded that patient requests for medicines are a powerful driver of prescribing decisions (Mintzes, et al, 2002).

The literature suggests that DTCA activities do have a significant and recognizable impact in terms of consumer attitudes, and information seeking behaviour. However, the arguments for and against DTCA remain largely theoretical, with little empirical substantiation. To-date however only one study has clearly linked DTCA with actual

changes in prescribing behaviour (Basara, 1996). Considering the high degree of interest in the potential for DTCA to impact prescription medication volume there is a need to replicate this research and extend findings to different markets This extension and replication of past research will provide important information for all parties involved with pharmaceutical DTCA.

## 2.8 Other Factors Influencing Pharmaceutical Sales Growth

In conclusion to this section, it is useful to consider the other factors potentially influencing pharmaceutical sales growth other than DTCA Factors such as changes to healthcare policy, increases in pricing, new products and technologies, new disease states, changing healthcare needs, and overall pharmaceutical promotion all have the potential to have a major impact on cost associated with sales of prescription medications in the pharmaceutical market. Understanding how these market elements can impact costs helps put the potential impact of DTCA into perspective, and puts the importance of assessing the potential for DTCA to impact prescription volumes into context.

### 2.8.1 Changes in Healthcare Policy

Government spending on medical care accounts for approximately 20% of all health and social service institutions expenditures, and is one of the fastest-growing components (Statistics Canada, 2002). Changes in healthcare policy such as increasing or limiting patient access to certain prescription medications have the potential to have a major

impact on the pharmaceutical market, particularly in terms of patient access to and reimbursement for prescription medications.

### 2.8.2 Pricing of Prescription Medications

The Patented Medicine Prices Review Board (PMPRB) controls prices of prescription medications in Canada. In 2000 the PMPRB indicated that manufacturers' prices of patented drugs in Canada increased slightly (+0.4%) from the previous year (Patented Medicine Prices Review Board, 2001). While pricing has held relatively constant in Canada due to PMPMRB restrictions and provincial government policies, this market element has the potential to have a major impact on future medication costs.

### 2.8.3 New Products and Technologies

The continued investment by pharmaceutical manufacturers in the improvement of medicines and the development of new and innovative treatments for illness has resulted in the introduction of many new products and technologies. In recent years, several blockbuster products have been introduced into unsatisfied markets in which existing competition was largely not promoted and available at a relatively low cost. The result has been a significant increase in the total spending to purchase these new alternatives.

### 2.8.4 New Diseases and Abilities to Diagnose

With the increased prevalence, and ability to diagnose illnesses there has been increased spending on treatments used to manage the symptoms and concomitant conditions associated with such illnesses. In recent past several new treatment options have been introduced onto the Canadian landscape representing true incremental costs to the system.

### 2.8.5 Changing Healthcare Needs

The changing healthcare needs of an aging population also drive costs upwards. The number of Canadians over the age of 65 is steadily increasing as the baby-boomer demographic segment begins to age. These Canadians often have more long-term and thus more expensive healthcare needs than other younger people.

### 2.8.6 Promotional Investment

The stimulation of demand via promotion of pharmaceutical products is thought to have had an impact on sales volumes. Spending on total promotion in the Canadian pharmaceutical market has increased in recent years, due in part to increased competition in major markets.

Clearly, increases in sales growth of prescription medications in Canada is related to a multitude of factors. While these factors include changes in healthcare policy, higher

prices, new products and technologies, new diseases and abilities to diagnose, changing healthcare needs, and increasing promotion, all of these elements are familiar and relatively predictable. The potential for consumer directed promotional activities by pharmaceutical manufacturers remains a topic of high interest to a variety of stakeholders due to its novelty, and potential to have an immediate and large impact on the Canadian pharmaceutical market.

# CHAPTER 3

# MATERIALS AND METHODS

## 3.1 Replication and Extension of Past Research

A replication and extension of previous research in the field of DTCA promotional response was utilized in order to make use of a validated and tested methodology, as well as provide a frame of reference for comparison purposes between the Canadian and U.S. markets. Components of research designed specifically to measure the impact of a DTCA campaign on new prescription volume (Basara, 1996), were selected for replication. This particular study was selected for replication because (1) it is the first empirical investigation of the impact of DTCA on new prescription volume, (2) extension of the findings of this research to a new market and new products category will provide insight into the findings, and (3) use of retrospective data available in both Canadian and U.S. markets, and time-series methodology make replication of methodology possible. However, in an attempt to replicate components of this study several limitations were identified which included:

- Basara's research made use of physician specific new prescription data. Restrictions relating to the availability, confidentiality, and release of physician specific information made this comparison in Canada impossible.

- Basara's research made use of test markets grouped according to metropolitan statistical area (MSA), a geographic area used by the United States census office, and

zip-code information. This grouping could not be performed in Canada due to the difficulty associated with relating the Canadian equivalent to MSA the census metropolitan area (CMA) to postal code forward sortation area (FSA) information. While the conversion of this information is possible, the means to perform this conversion were not available at the time of this research.

- Basara's research made use of an informational DTCA campaign for a migraine medication. A similar product example was not available due to the limited number of products for which DTCA has been used in the Canadian market

In order to overcome these limitations several modifications to the method used were required. These modifications which are described in detail later in this report however significant, do not affect the methodology used (e.g. intervention time-series) and thus should not negatively affect the ultimate goal of identifying and assessing the impact of DTCA.

## 3.2 Hypotheses

An increase in prescription volume is suggested to be the primary indicator of direct-to-consumer advertising success for the pharmaceutical industry (Drug Topics, 1985). The current study investigated changes in new prescription volume that occurred after an informational DTCA campaign had been initiated. The primary research hypothesis for the study is:

$H_1$: The number of new prescriptions for a prescription medication will increase significantly after consumers are exposed to a DTCA campaign for the medication.

A secondary hypothesis relating to the potential for regional differences in demographic characteristics of the target market is also proposed:

$H_2$: The change in number of new prescriptions for a prescription medication resulting from the exposure of consumers to a DTCA campaign will vary significantly according to regional differences.

In Basara's (1996) research an appropriate DTCA campaign was selected, four representative geographic areas of the United States were designated as sites from which the data were collected, and retrospective physician-level new prescription data (provided by IMS America) were aggregated at monthly intervals. Physician-level data refers to new prescription data collected at the actual individual physician level. New prescription data were used, rather than total prescriptions written during the period to minimize the effects of differences in refill amounts, treatment failures, and other confounding factors. A particular type of time-series analysis known as intervention analysis was applied to determine the nature and magnitude of differences in pre- and post-advertising prescription volume.

In this replication and extension of Basara's (1996) study one DTCA campaign was selected, and retrospective physician-level prescription data was replaced by provincial level prescription data. New prescription data was used for the same reasons as specified in the Basara (1996) research. A time-series analysis known as intervention analysis similar to the one used in the Basara (1996) research, was applied to determine the nature and magnitude of differences in pre- and post-advertising prescription volume.

## 3.3 Identification of a DTCA Campaign

The limited number of products for which DTCA has been used complicated the identification of an appropriate Canadian campaign. Basara (1996) specified criteria to be used in order to correctly identify a campaign that would provide results that were unencumbered by mitigating circumstances or a lack of data. Table 1 lists the criteria used by Basara (1996).

The rationale behind some of Basara's (1996) criteria is driven by the inherent characteristics of time-series analysis, which relies on historical data. However, the criteria regarding the prescription medications applicable to this type of analysis are unusual in that they suggest only products for which no significant competition exists. These criteria are restrictive considering the nature of the pharmaceutical market and the categories within.

Basara (1996) selected a product used to treat migraine (Imitrex) that was the only available treatment in its class. The product was launched in February 1993 and was supported by DTCA 11-months post launch in a campaign that lasted 7 months. Advertising for this product did not include product-specific print and/or television copy. Basara (1996) went on to say that:

"The absence of the product's brand name in the DTCA campaign has the potential to reduce the likelihood of product prescribing in response to patient visits to their physicians. At the time of the campaign, however, this product was the newest therapy available in a category consisting of old and relatively ineffective products. Additionally, because they are so old, most similar therapies are available generically and are not promoted to physicians on a regular basis" (Basara, 1996)

This is significant in that it suggests that the product example that Basara (1996) selected for this research was specific, and thus cannot necessarily be generalized to other markets with different characteristics.

The selection of Canadian DTCA campaigns that fit the Basara (1996) criteria for intervention time-series analysis was limited. Despite regulations, Canadian pharmaceutical marketers have managed to generate some direct-to-consumer marketing initiatives. Included in the broad definition of DTCA within the Canadian context are public relations initiatives, patient advocacy development, and full-scale patient directed media campaigns.

Public relations initiatives, in which product information released with the intention of using the media to disseminate new or interesting information to the general public as news is the most common form of DTCA in Canada. These types of communications are not subject to advertising restrictions and are particularly popular during the launch of a new product, or upon release of new clinical data regarding the characteristics of a product. The extent of this kind of activity however is difficult to measure and there is no formal Canadian monitoring agency at this time.

Some companies have worked with patient advocacy groups to focus communication efforts through direct-mail campaigns to patient members, or communicating new information concerning available treatments via such groups. Patient advocacy groups have a vested interest in working closely with the pharmaceutical industry, as it is one of the primary sources for funding, and is involved in efforts to encourage early diagnosis and effective treatment of diseases or medical conditions.

Large-scale media advertising campaigns have been relatively few. As previously mentioned, such campaigns are restricted to the promotion of a brand name, quantity, and price – or simply to an illness or condition. In recent past the latter has been the method of choice amongst Canadian pharmaceutical marketers. Some specific examples in table 3.1 include:

**Table 3.1: Canadian Direct-to-Consumer Advertising Campaigns**

| Company | Product | Timing | Condition |
|---|---|---|---|
| Hoffman-Laroche | Xenical | 1999 | Weight Loss |
| Pfizer | Viagra | 1999, 2000, 2001 | Erectile Dysfunction |
| Merck-Frosst | Propecia | 1999 | Male Pattern Baldness |
| GlaxoWellcome | Zyban | 1999, 2000, 2001 | Smoking Cessation |
| GlaxoWellcome | Imitrex | 1992 | Migraine |
| Schering | Diane-35 | 2000 | Acne Control |
| Wyeth-Ayerst | Alesse | 2000 | Oral Contraception |

Specific examples of some of the material used in these campaigns appear in Appendix 1, Appendix 2, Appendix 3, Appendix 4, and Appendix 5. Clearly from these examples, advertising for these products can be considered mainly informational, that is brand names were not used frequently, and when used were not associated with intended use of the product

Noteworthy, is that in each of these examples the products advertised using this method were for conditions for which there was either no existing prescription-only competition or the product being advertised had a significant and distinct advantage over other available alternatives. For example, for the treatment of erectile dysfunction at the time of the DTCA campaign there were no other prescription oral medications, and for the treatment of smoking cessation Zyban was the only new non-nicotine orally administered medication available. In the case of Alesse, this product was marketed in a category in which promotion was minimal, and products were not differentiated. Other products such as Xenical, Propecia, and Diane-35, while fitting some of Basara's (1996) criteria, are generally considered to appeal to niche markets and have relatively small prescription volumes and were thus not considered for time-series analysis.

### 3.3.1 The Alesse DTCA Campaign

Wyeth-Ayerst launched Alesse in January 1998. The substantial marketing investment placed behind Alesse was particularly interesting considering that the product was entering an already crowded oral contraception (OC) market. Furthermore, amongst existing OC's there were a significant number of generic competitors making the market highly sensitive to price. Alesse was promoted as offering the same protection against pregnancy as regular OC's with the added benefit of having a lower amount of active ingredient, which translated into an overall lower number of undesirable side effects such as weight-gain.

When marketing Alesse to consumers, Wyeth-Ayerst was faced with a problem. If Alesse was promoted indirectly using the importance of birth control, the company or product name could not be used in the advertisements thus would risk driving consumers to a competitor's OC's, or other available means of contraception. In an attempt to solve this problem Wyeth-Ayerst ran two ads, one shortly after the other. The first talked about the importance of birth control. The second featured Alesse, with no mention of what the product should be used for. The DTCA campaign was implemented nationally, involving television, print media, and billboards beginning in March 2000 and lasted until August 2000.

Wyeth-Ayerst specifically produced both a 30-second informational TV spot and a number of brand-focused advertisements. The branded advertisements consisted of two

15-second TV spots, a 60-second cinema ad and several posters that appeared in municipal transit systems. The two basic elements of the campaign - the informational spot and the various brand ads - were distributed to the public in the same time frame, spring through summer 2000. The informational TV ad and the 15-second TV brand ads were intended to air in rotation first on MuchMusic and in the fall on network television All the ads were focused on the same basic theme, learning lessons and being wise in relationships (National Post, 2000).

In response to the Alesse campaign, Health Canada issued a policy statement stating that running two separate ads, that taken together violate the regulations, is prohibited (Montreal Gazette, 2001). This change in policy however, did not affect the Alesse campaign, which was completed in September 2000.

### 3.3.2 The Viagra DTCA Campaign

Pfizer launched Viagra in March 1998, which IMS Health Canada reports at the time held the fastest adoption of a new product in Canada, effectively making it a blockbuster product. After a full three months on the market Viagra sales totaled $13,306,000. (IMS Health Canada Inc, 1999). Viagra the first oral prescription medication for the treatment of erectile dysfunction was the first orally administered treatment for the effects of psychologically or physiologically induced erectile dysfunction. Competition to Viagra was primarily in the device market; while there was some competition from other prescription medications administered by injection and did not compete directly in the oral segment. Bolstering the launch success of Viagra was thought to be the U.S. launch

of the product that had occurred several months prior. The launch in the U.S. was accompanied by a significant promotional and public relations investment.

Pfizer Canada Inc. introduced a 5-month DTCA for Viagra in October 1999 with an unbranded campaign designed to increase awareness of erectile dysfunction under the name of EDCare Canada. The campaign made extensive use of web sites, magazine ads with business reply cards and a 1-800 telephone number.

In spring/summer 2001 Pfizer Canada Inc. continued its efforts in support of Viagra via unbranded DTCA using a large-scale television campaign, and in the Fall of 2001 with a televised testimonial of the merits of discussing ED with a doctor featuring a well-known Canadian hockey player. Beginning in January 2002 Pfizer Canada Inc. has launched a branded television advertising Campaign featuring a 'Good Morning' theme with no mention of product features or uses.

### 3.3.3 The Zyban DTCA Campaign

GlaxoWellcome launched Zyban in August 1998 which IMS Health Canada reports, at the time held the second fastest adoption of a new product in Canada. After a full three months on the market Zyban sales totaled $9,071,000 (IMS Health Canada Inc, 1999). Zyban, the first nicotine-free prescription pill to help people quit smoking, was originally developed and marketed as a prescription anti-depressant known as Wellbutrin. Researchers found during clinical trials that people taking Zyban also lost the urge to

smoke. The manufacturer also claimed that subjects put on half as much weight after quitting smoking using Zyban than other products. Competition to Zyban was primarily in the nicotine-replacement market, much of which was over-the-counter and sold in a chewable or transdermal (patch) formulation.

Approximately 6-months post–launch GlaxoWellcome released an unbranded informational DTCA campaign which appeared as advertisements from the Lung Association and Physicians for a Smoke-Free Canada. The advertisements appeared in newspapers, on television and in magazines across Canada. The advertisements suggested that people ask their doctors about oral smoking cessation products. The campaign began at the beginning of January, the most popular month for Canadian smokers to attempt to stop smoking and thus request smoking cessation medications from their physicians. The campaign ran for three-months at an estimated cost of $1-million (National Post, 1999).

GlaxoWellcome continued its investment in DTCA in support of Zyban in 2000. In 2000 the campaign included television ads run between January and March including a testimonial where a person is talking about addiction to smoking which ends with the brand name Zyban being flashed across the screen (Undercurrents, 2001).

In 2001, GlaxoWellcome continued to advertise Zyban during the peak smoking-cessation period with a DTCA campaign that included 197 billboards up in major cities

across Canada including the Zyban brand name and depicting a smiling couple in bed, a party hat and a coffee cup (Halifax Daily News, 2001).

GlaxoWellcome issued serious health concerns to Zyban users in mid-2001, after several serious adverse effects were directly related to the products use. These warnings are thought to have had a negative impact on Zyban usage. Despite the negative publicity received by GlaxoWellcome regarding the potentially serious adverse events associated with Zyban use, DTCA for the product continued into 2002.

All DTCA initiatives for Zyban have been focused during the peak period for smoking cessation attempts, which typically occur during December to March to coincide with the setting of New Year's resoloutions.

### 3.3.4 Selection of a DTCA Campaign

Clearly, examples of Canadian DTCA are not representative of Basara's (1996) criteria for the types of campaigns for which intervention time-series analysis may be considered appropriate. More specifically, Canadian DTCA has been used almost exclusively for products considered blockbusters (e.g. Viagra, Zyban) or for products that appeal to a lifestyle or cosmetic concern (e.g. Xenical, Propecia). This selective use of DTCA however reflects the reality in the Canadian pharmaceutical market.

Wyeth-Ayerst's DTCA campaign in support of Alesse was selected for the focus of intervention time-series analysis. The Alesse campaign most closely met Basara's criteria due to the fact that this product represented a significant improvement over existing alternatives, and there were relatively low levels of promotion of competing products in Canada. In addition, data related criteria were met in that this was the first DTCA initiative for this product, and it occurred at least 6-months after the product was launched. Finally, while this campaign did mention the product brand name without mention of the intended use, use of the product format in the ad (appendix 1) suggested its use as an oral contraceptive.

### 3.4 Identification of Test Markets

In Basara's (1996) research four demographically similar geographic areas (known as metropolitan statistical areas or MSAs) were identified to serve as sites for data analysis. To ensure that groups of physicians and consumers were as similar as possible prior to the introduction of the DTCA campaign MSAs were clustered on the basis of demographic similarity, and physician activity was monitored to ensure a normal distribution of high, medium, and low, use of prescription medications.

For several reasons previously stated, Basara's (1996) approach was not possible in the Canadian context. First, IMS Health Canada does not provide physician level prescribing data due to stringent confidentiality and privacy restrictions in Canada. Rather, this information is available to the pharmaceutical industry aggregated at the decile level.

which is not sufficient for the intended use of intervention time-series analysis. Second, in the case where this kind of information/data would have been available, IMS Health Canada does not categorize this information by the Canadian equivalent of an MSA. More specifically, this data is categorized at the postal code or forward sortation area (FSA) level that does not easily translate into Statistics Canada standard geographical unit known as a Census Metropolitan Area (CMA). Finally, in the case where these two obstacles could have been overcome, the availability of such data for periods prior to the year 2001 is extremely limited and the reliability is not well established.

In order to overcome the above-mentioned limitations an alternative approach was used. IMS Health Canada Compuscript© provincial level prescription data was used. CompuScript© measures the retail outflow of prescriptions, or the rate at which drugs move out of independent, chain and independent pharmacies into the hands of consumers via formal prescriptions. IMS Health Canada currently collects data from over 3,500 pharmacies nationwide, and over 2,300 pharmacies are used in the CompuScript© sample. CompuScript© data is projected and measures medications dispensed by the pharmacist to the consumer.

### 3.5 Region Identification

IMS Health Canada maintains a panel of computerized retail pharmacies stratified by region, type (chain/independent) and size. From these pharmacies, records are collected on every new and refill prescription transaction taking place throughout the month. The

collection process takes place using centralized computers in several locations across Canada, where prescription data are gathered from participating pharmacies on a continuous basis. The IMS Health Canada universe consists of all retail independent, and chain pharmacies operating in Canada. The Figures are updated on a semi-annual basis.

The sample data is projected to the universe by cell in each province. The sample pharmacies and the universe stores are both stratified by province, type, and size. This stratification defines the 40 projection cells (10 provinces x 2 types x 2 sizes). The projection methodology involves calculating a universe divided by sample projection factor for each projection cell and applying this factor to the raw data. Collapsing of cells according to statistically valid parameters becomes necessary in cases where reporting sample store counts fall below pre-set minimums.

There are 9 provinces in Canada; of these provinces 3 with 20% or higher sampling coverage rate by IMS Health Canada as of December 2000 were selected for statistical analysis. The IMS sampling coverage rate is the proportion of pharmacies in the province reporting prescription data to IMS Health Canada each month. The 60% minimum as per Basara's (1996) specifications ensures acceptable coverage for statistical analysis. This standard cannot apply to the Canadian market as IMS Health Canada only includes approximately 30% of pharmacies in the National sample.

Considering the 20% minimum the provinces applicable for further analysis included Ontario, Quebec, Alberta, and the Atlantic provinces (Table 3.2). For provincial

comparison and selection consumer demographics of interest included gender, age, and mother tongue/language.

**Table 3.2: IMS HEALTH CANADA – Sampling for Rx Projection by Province**

| | 2000 Average Sample | 2000 Average Universe | Coverage |
|---|---|---|---|
| **Quebec** | 875 | 1,575 | 55.6% |
| **Ontario** | 841 | 2,603 | 32.3% |
| **Alberta** | 165 | 779 | 21.2% |
| **National** | 2,280 | 6,948 | 32.8% |

The provinces Ontario, Quebec, and Alberta were chosen for test markets due to IMS Health Canada's sampling rate and relatively large population bases in these provinces

While the focus of the research was determined to be the DTCA campaign supporting Alesse, data for both Viagra and Zyban were requested for further analysis.

To summarize IMS Health Canada provided Compuscript© new prescription data nationally and for selected provinces aggregated at monthly intervals for the period January 1998 to June 2001.

### 3.6 Demographic Differences

For provincial comparison and selection consumer demographics of interest included gender, age, and mother tongue/language. Statistics Canada (1996) census data was obtained for Canada, Quebec, Ontario, and Alberta in order that regional differences in

DTCA impact could be explored. Table 3.3 includes population, gender, language, and age estimates.

**Table 3.3: Statistics Canada 1996 Census – National and Regional Demographics**

| | Statistics Canada 1996 Census: 20% Sample | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | CANADA | | QUEBEC | | ONTARIO | | ALBERTA | |
| **Total** | **28,528,125** | **100.0%** | **7,045,080** | **100.0%** | **10,642,790** | **100.0%** | **2,669,195** | **100.0%** |
| | | | | | | | | |
| **Male** | 11,022,455 | 38.6% | 2,756,705 | 39.1% | 4,080,940 | 38.3% | 1,021,430 | 38.3% |
| **Female** | 11,606,470 | 40.7% | 2,916,760 | 41.4% | 4,348,275 | 40.9% | 1,033,585 | 38.7% |
| | | | | | | | | |
| **English** | 16,890,615 | 59.2% | 586,435 | 8.3% | 7,694,635 | 72.3% | 2,159,275 | 80.9% |
| **French** | 6,636,660 | 23.3% | 5,700,150 | 80.9% | 479,285 | 4.5% | 52,380 | 2.0% |
| **Multi-Res.** | 402,560 | 1.4% | 100,920 | 1.4% | 172,300 | 1.6% | 33,725 | 1.3% |
| **Other** | 4,598,290 | 16.1% | 657,580 | 9.3% | 2,296,570 | 21.6% | 423,810 | 15.9% |
| | | | | | | | | |
| **Ttl 15yr+** | 22,628,925 | 79.3% | 5,673,465 | 80.5% | 8,429,215 | 79.2% | 2,055,020 | 77.0% |

Between Ontario, Quebec, and Alberta population sizes are significantly different and regional differences exist in terms of mother tongue/language. Based on the results of intervention time-series analysis, these regional differences can be used to answer the secondary hypothesis, and provide insight into possible reasons for regional differences in the impact of DTCA, if any.

## 3.7 Time-Series Analysis

Time-series data are observations that are made or measured at equally spaced points in time. Analysis of time-series data allows one to understand and forecast the dynamic nature of the relationship between a study variable and time (Campbell and Stanley, 1966). A common research question in time series analysis is whether an outside event

affected subsequent observations, this type of interrupted time-series analysis is described in detail by McDowall, McCleary, Meidinger, & Hay (1980). With the introduction of time-series analysis, the relationship between a study variable and time could be modeled, while including effects of all other variables that influence the model (Box and Jenkins, 1976). Box-Jenkins models are also known as autoregressive integrated moving average (ARIMA) models. The general process of modeling time-series data involves the identification of an appropriate ARIMA model, fitting the model to empirical data, and assessing the model's accuracy.

For this study, as in Basara's (1996) study an intervention (i.e., the DTCA campaign) is known to occur over the time period. The research question is focused on determining evidence of an increase in new prescriptions resulting from the campaign. A particular time-series technique known as intervention time-series analysis can be used to determine the existence, magnitude, and nature of the change in new prescriptions resulting from the campaign (Box and Tiao, 1975).

## 3.8 Regression Model with ARIMA Noise Determination

To understand the applications of regression models with ARIMA noise, it is important to realize the nature of time-series data. Consider the nature of sales fluctuations over time; seasonality, the economy, marketing strategies, and other factors influence sales performance. A regression model with ARIMA noise can mathematically describe the nature of this influence.

Each of three types of mathematical processes; autoregression, integration or differencing, and moving average, can be used alone or together to describe the way in which data respond to disturbances. The general ARIMA model is noted as ARIMA $(p,d,q)$, where $p$ is the order of auto-regression, $d$ is the degree of differencing, and $q$ is the order of moving average.

Any time-series of data that includes a discrete intervention or event may be categorized into two series of data – pre-intervention and post-intervention. Analysis of these two series of data via a statistical comparison requires a statistical model.

$Y_t = b_{pre} + b_{post} + e_t$

Where

$Y_t$ = the $t^{th}$ observation of a time-series

$b_{pre}$ = the pre-intervention series level

$b_{post}$= the post-intervention series level

$e_t$ = an error series associated with $Y_t$

The null hypothesis of this model,

$H_0$: $b_{pre} - b_{post} = 0$

States that there is no statistically significant difference between the pre- and post-intervention series levels. That is that the intervention had no statistically significant impact on the series level.

Autocorrelation of time-series data must be addressed before data analysis can begin. Autocorrelation occurs when residual error terms from observations of the same variable change as their separation increases (Box, Jenkins, 1976). In regression modeling, autocorrelation can lead to relatively inefficient estimates of regression coefficients, underestimation of the true variance of error terms, and difficulty using standard procedures for estimating confidence intervals. When data modeled using regression methods are affected by autocorrelation, ARIMA procedures can be applied to mathematically manage subsequent problems.

To identify the extent of autocorrelation and other types of systematic error in preparation for ARIMA two types of coefficients are relevant. Autocorrelation coefficients (AC) and partial autocorrelation coefficients (PAC) are calculated for a data series at each time period or lag. AC's indicate whether errors associated with variables that are a certain number of time periods (lags) apart relate to each other. PAC's control for autocorrelation at intervening time lags (Makridakis and Wheelwright, 1978).

After evaluation of the AC and PAC plots and preliminary identification of $p$, $q$, and $d$, coefficients of a regression model with ARIMA noise are estimated. The final step is to evaluate the error series associated with the calculated regression model with ARIMA noise. When the series appeared stationary and the autocorrelation coefficients were not different from Zero using the Box-Ljung statistic (i.e. the series is white noise), the model is correctly specified (SPSS/PC+, 1990).

## 3.9 Intervention Analysis

Because this and Basara's (1996) research is focused on the specific effect of a known intervention (i.e. a DTCA campaign), during the time-period of interest the regression model with ARIMA noise was adapted to include the intervention. The intervention is represented as a binary variable which is "0" prior to the intervention and "1" during the intervention.

In Basara's (1996) research the response to the intervention was expected to include a lagged component due to the assumption that advertising spending would have both an immediate and delayed impact on product sales. Basara's (1996) assumed that a gradual increase in new prescriptions for the advertised product occurred during the period over which the campaign was implemented. Basara (1996) used impulse response weights, defined as the intervention variable coefficient to estimate the DTCA campaign's short- and long-term effects on new prescription volume.

# CHAPTER 4

# RESULTS AND ANALYSIS

## 4.1 Time-Series Analysis

Upon province selection, IMS Health Canada Compuscript© new prescription data for Alesse, Viagra, and Zyban were provided for each province for the 42-month time period between January 1998 and December 2001. For each product, data were aggregated to form three different data series by province, which were then used for time series analysis.

## 4.2 Alesse Intervention Time-Series Analysis

IMS Health Canada new prescription data for Alesse appear in Figures 4.1 and 4.2. Examination of the data series suggests a seasonal pattern to the distribution of the series

**Figure 4.1: Alesse New Prescription Volume – Ontario, Quebec, Alberta**

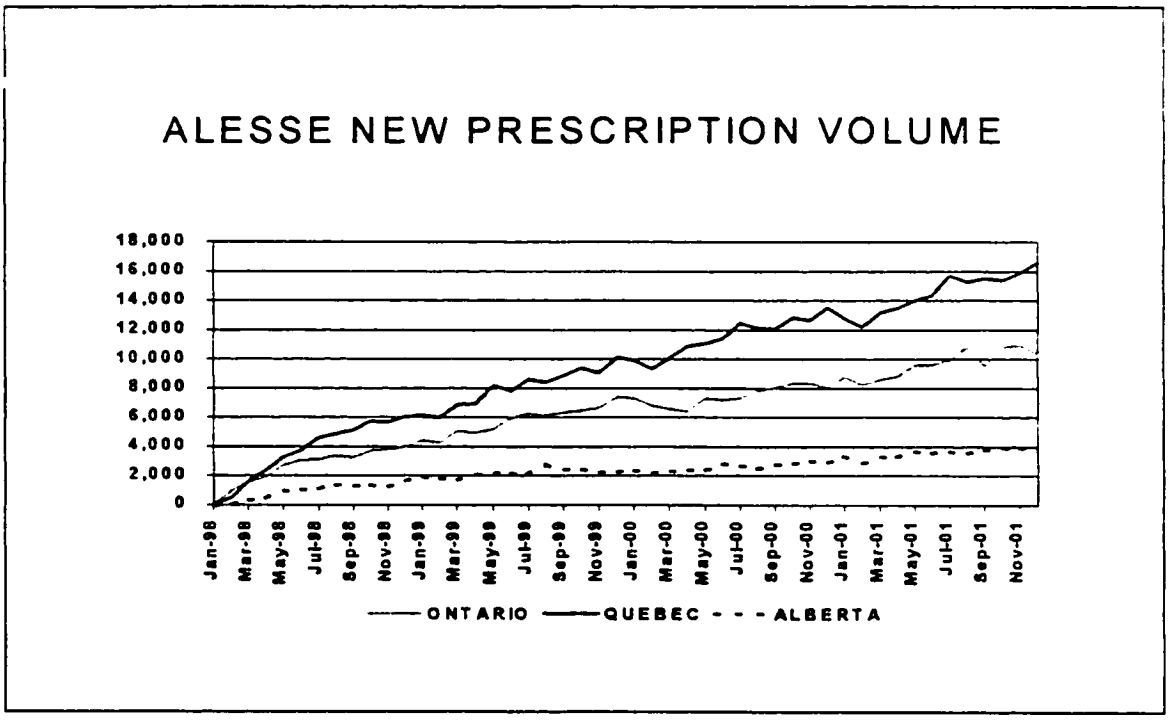
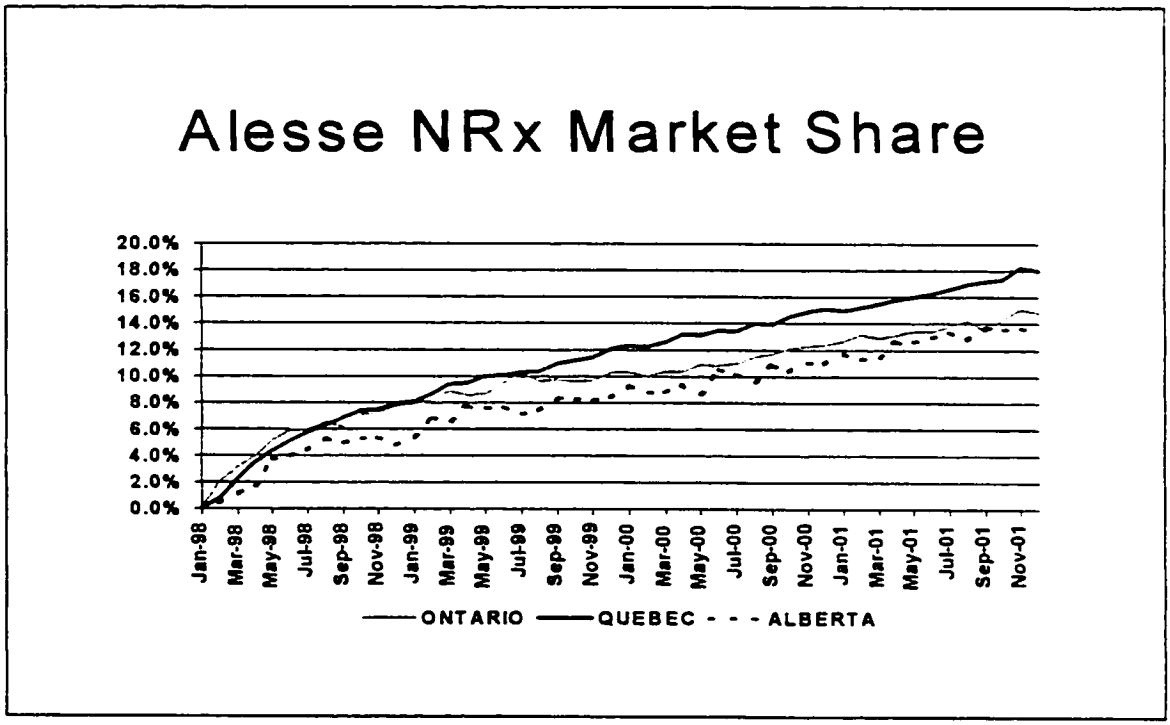



**Figure 4.2: Alesse New Prescription Share – Ontario, Quebec, Alberta**

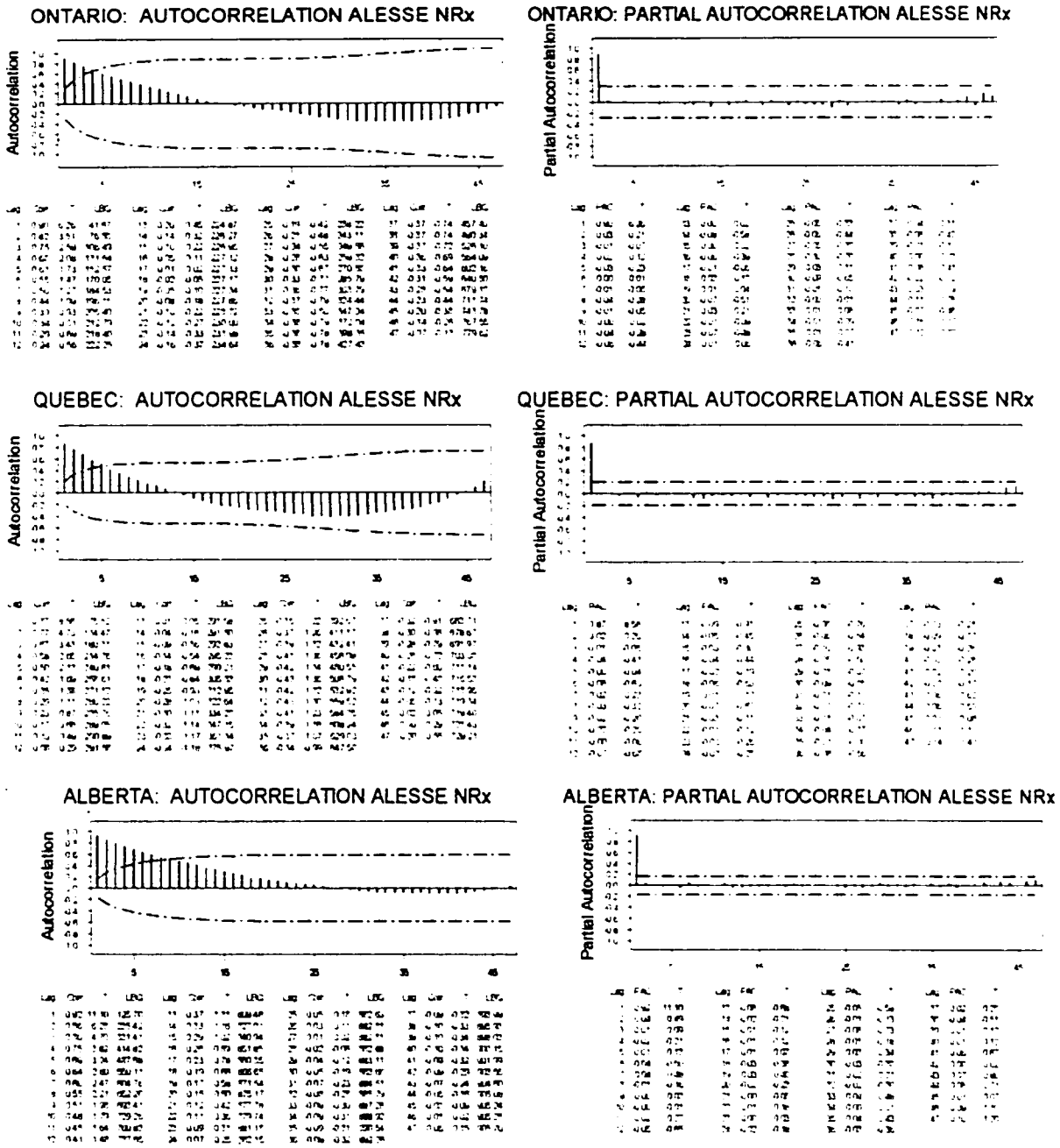


The first step in time-series analysis is the *Identification* of an appropriate ARIMA model. The input series for ARIMA modeling needs to be stationary, that is, it should have a constant mean, variance, and autocorrelation through time. Therefore, often a time-series needs to be differenced until it is stationary. In order to determine the necessary level of differencing examination of the time-series plot (Figure 4.1), autocorrelation, and partial autocorrelation plots (Figure 4.3) was used.

The dotted lines in the plots of the partial autocorrelation plot are the approximate two standard error bounds. If the partial autocorrelation is within these bounds, it is not significantly different from zero at (approximately) the 5% significance level.

To determine the appropriate level of differencing from the time-series plot, it is noted that significant changes in level (strong upward or downward changes) usually require first-order differencing and strong changes in slope usually require second order differencing. From the autocorrelation plot, if autocorrelation coefficients decline slowly at longer lags first order differencing is usually needed.

**Figure 4.3: Alesse Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta**




It is also necessary to determine the number of autoregressive ($p$) and moving average ($q$) parameters necessary to yield an effective model of the process including the least number of parameters and greatest number of degrees of freedom. The $p$ term

corresponds to the use of a lagged value of the residual in the forecasting equation for the unconditional residual. The $q$ term corresponds to the use of lagged values of the forecast error to improve the forecast. This process is not straightforward and requires some experimentation with alternative models.

It is noted that many time-series patterns can be sufficiently approximated using one of the 5 basic models that can be identified based on the shape of the autocorrelation AC and partial autocorrelation PAC plots (Pankratz, 1983).

1. One autoregressive (p) parameter: ACF – exponential decay; PACF – spike at lag 1, no correlation for other lags
2. Two autoregressive (p) parameters: ACF – a sine-wave shape pattern or a set of exponential decays; PACF – spikes at lags 1 and 2, nor correlation for other lags
3. One moving average (q) parameter: ACF – spike at lag 1, no correlation for other lags; PACF – damps out exponentially.
4. Two moving average (q) parameters: ACF – spikes at lags 1 and 2, no correlation for other lags; PACF – a sine-wave shape pattern or a set of exponential decays.
5. One autoregressive (p) and one moving average (q) parameter: ACF – exponential decay starting at lag 1; PACF – exponential decay starting at lag 1.

In cases where there is a systematic pattern inherent in the data series seasonal ARIMA models need to be considered. The general recommendations concerning the selection of parameters to be estimated (based on AC and PAC), also apply to seasonal models. The main difference is that in seasonal models, AC and PAC will show sizeable coefficients at multiples of the seasonal lag.

Based on the above considerations, and after considering the coefficients of determination ($R^2$), F-values, and significance levels of several alternative regression models, one with 0 differencing (d), 0 moving average (q) parameters, 0 seasonal moving average parameter (sq), 1 autoregressive (p) parameters, and 1 seasonal (sp) autoregressive parameters was appropriate for each of the series: (p,d,q)(sp,sd,sq) = (1,0,0)(1,0,0).

NRx Volume = DTCA + C + NRX(-1) + AR(1) + SAR (1)

To justify the (0,0,1)(0,0,1) model selection it is important to determine whether or not the residuals of the model are stationary and significantly different from zero using the Box-Ljung statistic. If there is no serial correlation in the residuals, the AC's and PAC's at all Lags should be nearly zero, and all Box-Ljung Q-statistics should be insignificant with large p-values.

The Box-Ljung Q-statistics suggests that the error series associated with the calculated ARIMA models were stationary and none of the values were significantly different from zero (Table 4.1). The Durbin-Watson statistics measures first-order correlation amongst residuals to determine whether or not serial correlation is affecting the model. Durbin-Watson statistics are close to 2 (Table 4.2, 4.3, and 4.4) suggest that there is no serial correlation amongst residuals.

Finally, high $R^2$ and adjusted $R^2$ values (Tables 4.2, 4.3, and 4.4), which measure the success of the regression in predicting the value of the dependent variable, suggest that

the ARIMA (1,0,0)(1,0,0) model was correctly specified. Finally, the F-statistic measures the probability that all coefficients excluding the constant and intercept are zero.

**Table 4.1: Alesse Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta ARIMA (1,0,0)(1,0,0) Model**

| | Ontario | | | | | Quebec | | | | | Alberta | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob |
| 1 | 0.001 | 0.001 | 4.E-05 | | 1 | -0.099 | -0.099 | 0.3655 | | 1 | -0.097 | -0.097 | 0.3503 | |
| 2 | -0.113 | -0.113 | 0.4901 | | 2 | -0.215 | -0.227 | 2.1369 | | 2 | -0.231 | -0.243 | 2.3918 | |
| 3 | 0.099 | 0.101 | 0.8804 | 0.348 | 3 | 0.054 | 0.006 | 2.2523 | 0.133 | 3 | -0.069 | -0.129 | 2.5774 | 0.108 |
| 4 | -0.024 | -0.039 | 0.9041 | 0.636 | 4 | 0.098 | 0.060 | 2.6468 | 0.266 | 4 | 0.194 | 0.122 | 4.1193 | 0.127 |
| 5 | 0.089 | 0.116 | 1.2420 | 0.743 | 5 | -0.348 | -0.338 | 7.7586 | 0.051 | 5 | -0.062 | -0.072 | 4.2840 | 0.232 |
| 6 | -0.057 | -0.082 | 1.3861 | 0.847 | 6 | -0.064 | -0.126 | 7.9377 | 0.094 | 6 | 0.019 | 0.074 | 4.2998 | 0.367 |
| 7 | -0.201 | -0.173 | 3.2164 | 0.667 | 7 | 0.143 | -0.023 | 8.8642 | 0.115 | 7 | -0.024 | -0.014 | 4.3265 | 0.503 |
| 8 | -0.115 | -0.158 | 3.8363 | 0.699 | 8 | 0.013 | -0.016 | 8.8725 | 0.181 | 8 | -0.157 | -0.198 | 5.4890 | 0.483 |
| 9 | 0.132 | 0.120 | 4.6833 | 0.699 | 9 | -0.063 | -0.003 | 9.0653 | 0.248 | 9 | -0.017 | -0.046 | 5.5034 | 0.599 |
| 10 | 0.000 | -0.003 | 4.6833 | 0.791 | 10 | -0.108 | -0.267 | 9.6560 | 0.290 | 10 | 0.212 | 0.121 | 7.7958 | 0.454 |
| 11 | -0.125 | -0.070 | 5.5121 | 0.788 | 11 | 0.165 | 0.052 | 11.097 | 0.269 | 11 | -0.004 | 0.005 | 7.7968 | 0.555 |
| 12 | -0.238 | -0.277 | 8.6714 | 0.564 | 12 | -0.152 | -0.210 | 12.383 | 0.260 | 12 | -0.109 | 0.014 | 8.4585 | 0.584 |
| 13 | -0.127 | -0.172 | 9.6100 | 0.566 | 13 | 0.090 | 0.137 | 12.859 | 0.303 | 13 | 0.003 | 0.014 | 8.4591 | 0.672 |
| 14 | 0.106 | -0.004 | 10.304 | 0.589 | 14 | 0.043 | -0.023 | 12.970 | 0.371 | 14 | 0.008 | -0.078 | 8.4630 | 0.748 |
| 15 | 0.046 | 0.066 | 10.443 | 0.657 | 15 | -0.006 | -0.139 | 12.973 | 0.450 | 15 | -0.092 | -0.113 | 9.0042 | 0.773 |
| 16 | -0.157 | -0.110 | 12.125 | 0.596 | 16 | -0.148 | -0.117 | 14.460 | 0.416 | 16 | -0.005 | -0.069 | 9.0058 | 0.831 |

**Table 4.2: Alesse – Ontario ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Ontario NRx Volume
**Method: Least Squares**
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -453.7262 | 159.3667 | -2.847057 | 0.0080 |
| **C** | 7063.468 | 2750.245 | 2.568305 | 0.0156 |
| **Lagged NRx** | 0.527881 | 0.166831 | 3.164176 | 0.0036 |
| **Autoregressive (1)** | -0.173887 | 0.224528 | -0.774457 | 0.4449 |
| **Seasonal AR(12)** | 0.753551 | 0.069212 | 10.88752 | 0.0000 |
| **R-squared** | 0.941338 | **Mean (NRx)** | | 7818.353 |
| **Adjusted R-squared** | 0.933246 | **S.D. (NRx)** | | 1685.188 |
| **Log likelihood** | -252.1327 | **F-statistic** | | 116.3383 |
| **Durbin-Watson** | 1.983866 | **P-Value** | | 0.000000 |

**Table 4.3: Alesse – Quebec ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Quebec NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 25.98370 | 82.59838 | 0.314579 | 0.7553 |
| **C** | 14810.89 | 5184.360 | 2.856840 | 0.0078 |
| **Lagged NRx** | 0.643445 | 0.132915 | 4.841043 | 0.0000 |
| **Autoregressive (1)** | -0.493935 | 0.182239 | -2.710376 | 0.0112 |
| **Seasonal AR(12)** | 0.896519 | 0.050663 | 17.69569 | 0.0000 |
| **R-squared** | 0.984859 | **Mean (NRx)** | | 11681.79 |
| **Adjusted R-squared** | 0.982770 | **S.D. (NRx)** | | 2775.038 |
| **Log likelihood** | -246.0673 | **F-statistic** | | 471.5668 |
| **Durbin-Watson** | 2.143649 | **P-Value** | | 0.000000 |

**Table 4.4: Alesse – Alberta ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Alberta NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -2.634529 | 69.23174 | -0.038054 | 0.9699 |
| **C** | 81.22990 | 134.6192 | 0.603405 | 0.5509 |
| **Lagged NRx** | 0.991699 | 0.045229 | 21.92608 | 0.0000 |
| **Autoregressive (1)** | -0.585222 | 0.151810 | -3.854964 | 0.0006 |
| **Seasonal AR(12)** | 0.043574 | 0.182576 | 0.238663 | 0.8130 |
| **R-squared** | 0.890297 | **Mean (NRx)** | | 2862.912 |
| **Adjusted R-squared** | 0.875165 | **S.D. (NRx)** | | 639.5051 |
| **Log likelihood** | -229.8305 | **F-statistic** | | 58.83724 |
| **Durbin-Watson** | 2.132161 | **P-Value** | | 0.000000 |

In Tables 4.2, 4.3, and 4.4 the standard error column reports the estimated standard errors of the coefficient estimates. The standard errors measure the statistical reliability of the coefficient estimates. The larger the standard errors, the more statistical noise in the estimates.

The t-statistic, which is computed as the ratio of an estimated coefficient to its standard error, is used to test the hypothesis that a coefficient is equal to zero. To interpret the t-statistic, the probability of observing the t-statistic given that the coefficient is equal to zero needs to be assessed.

The last column of the output shows the probability of drawing a t-statistic similar to the one actually observed, under the assumption that the errors are normally distributed, or that the estimated coefficients are asymptotically normally distributed. This probability is also known as the p-value or the marginal significance level. The p-value is used to determine whether or not to accept the hypothesis that the true coefficient is zero against a two-sided alternative that it differs from zero.

The analysis indicate that the Alesse data does not demonstrate an impact of the DTCA initiative on new prescription volume in Ontario, Quebec, or Alberta. More specifically, the DTCA parameter is not different from 0 in any of the major markets studied. As a result the primary research hypothesis for the study fails:

$H_1$: The number of new prescriptions for a prescription medication will increase significantly after consumers are exposed to a DTCA campaign for the medication.

The secondary hypothesis relating to the potential for regional differences to affect the number of new prescriptions also fails.

$H_2$: The change in number of new prescriptions for a prescription medication resulting from the exposure of consumers to a DTCA campaign will vary significantly according to regional differences.

An investigation of possible causes for the failure of the primary hypothesis of the study was carried out. More specifically, an ARIMA time-series intervention analysis for the two leading competitors of Alesse was performed to determine whether or not DTCA in support of Alesse had an impact on prescription trends for the two leading prescription medications in the oral contraceptive market.

Additional IMS Health Canada Compuscript© new prescription data was obtained for the two leading oral contraceptives available in Canada, Tri-cyclen and Triphasil, for the time period January 1998 to December 2001. New prescription data for the two additional products was used to generate series of data (1) Tri-cylen alone, (2) Triphasil alone, and (3) Tri-cyclen, Triphasil, and Alesse combined, for the provinces Ontario, Quebec, and Alberta.

IMS Health Canada new prescription data for the three series appear in Figures 4.4, 4.5, and 4.6.

**Figure 4.4: Tri-cyclen New Prescription Volume – Ontario, Quebec, Alberta**

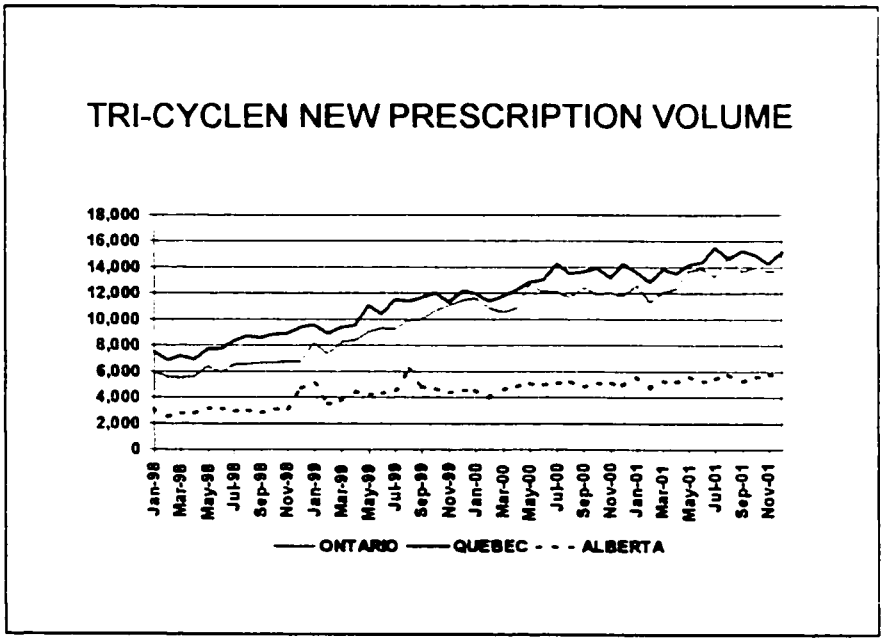



**Figure 4.5: Triphasil New Prescription Volume – Ontario, Quebec, Alberta**

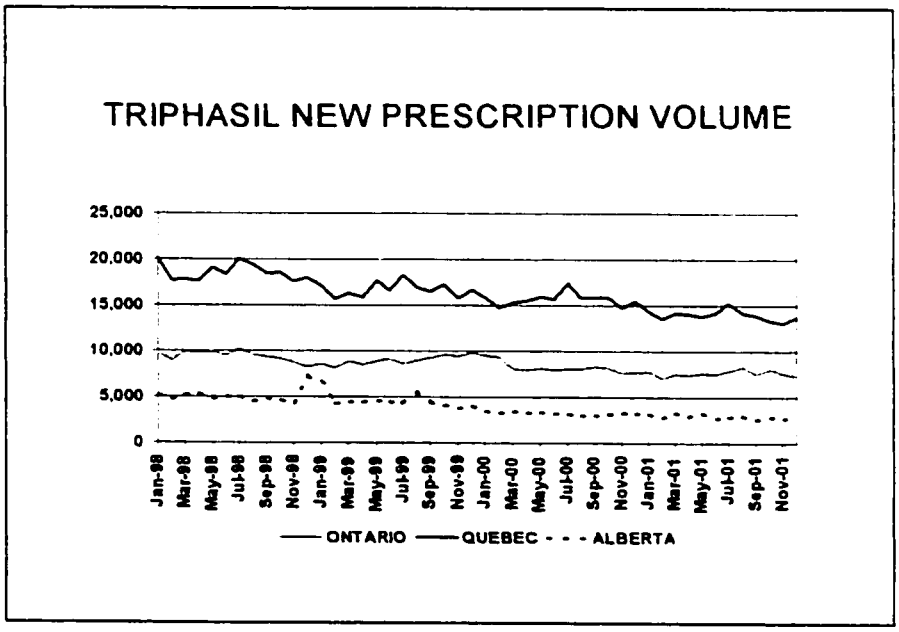
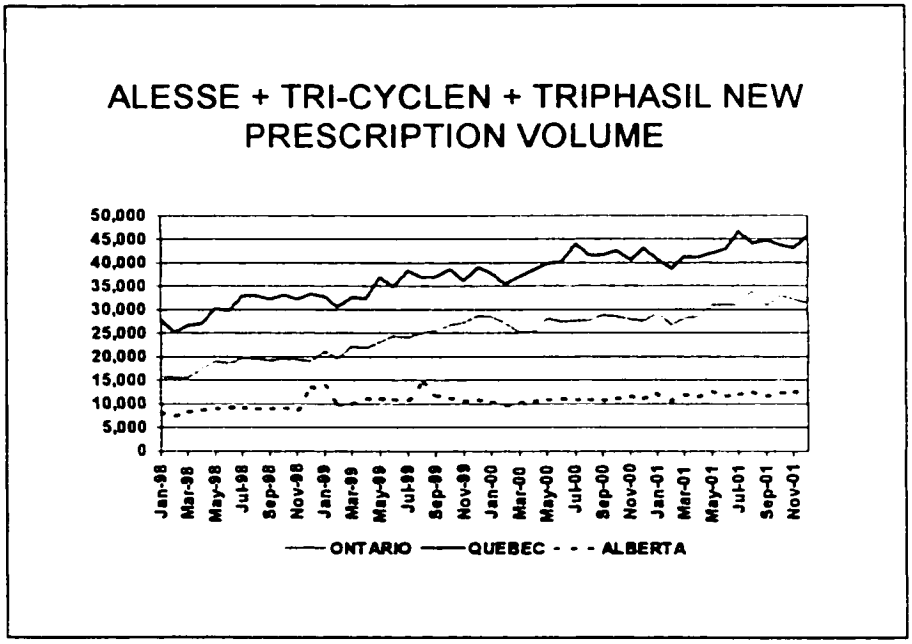


**Figure 4.6: Alesse + Tri-cyclen + Triphasil New Prescription Volume – Ontario, Quebec, Alberta**



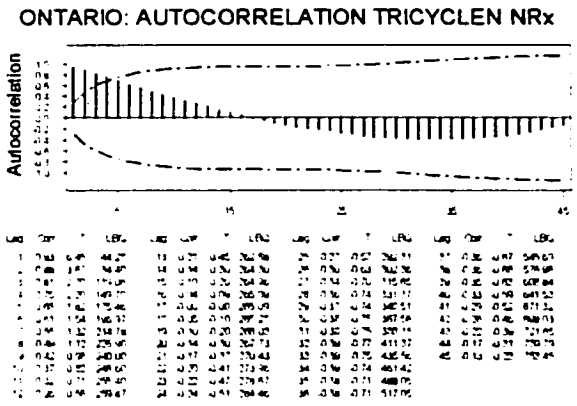

Examination of prescription trends in Figures 4.4, 4.5, and 4.6 suggests evidence of the seasonal pattern apparent in the Alesse series. The *Identification* of an appropriate ARIMA model for the new series followed the same steps as in the initial examination of the Alesse series. Examination of the autocorrelation and partial autocorrelation plots (Figures 4.7, 4.8, and 4.9) suggests that the input series can be considered stationary and following a similar seasonal pattern to the Alesse series. Based on these considerations, and after considering the coefficients of determination ($R^2$), F-values, and significance levels of several alternative regression models, one with 0 differencing (d), 0 moving average (q) parameters, 0 seasonal moving average parameter (sq), 1 autoregressive (p)

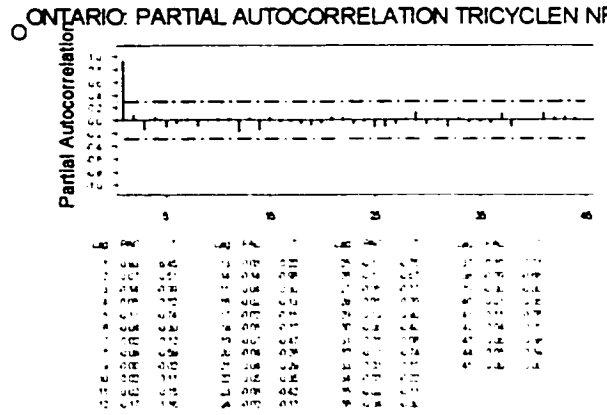
parameters, and 1 seasonal (sp) autoregressive parameters was appropriate for each of the series: (p,d,q)(sp,sd,sq) = (1,0,0)(1,0,0).

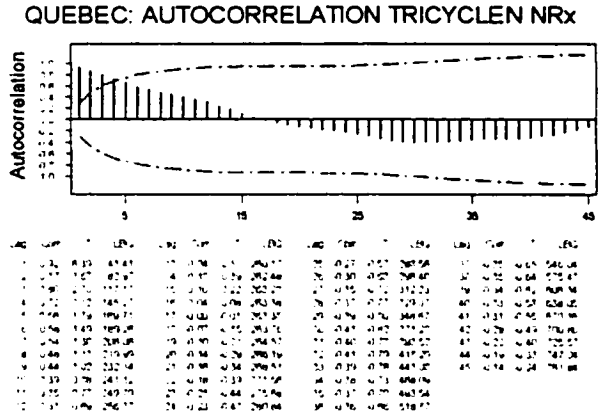
NRx Volume = DTCA + C + NRX(-1) + AR(1) + SAR (1)

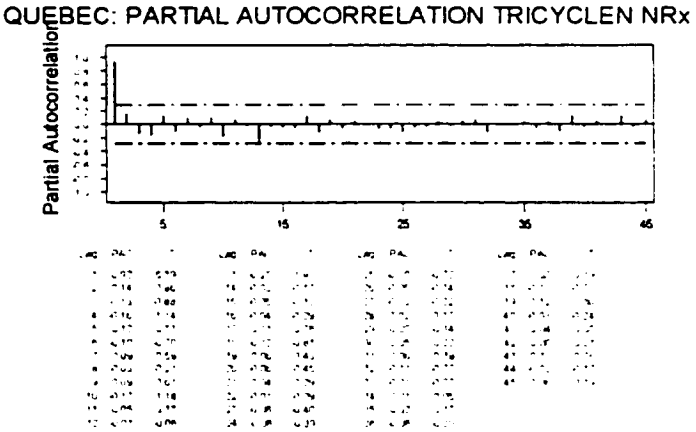
Results (tables 4.5 to 4.16) suggest that this model is correctly specified for each of the series. Specifically, the Box-Ljung Q-statistics were not significantly different from zero and the Durbin-Watson statistics are close to 2 suggesting that there is no serial correlation amongst residuals. Finally, high $R^2$ and adjusted $R^2$ values, and the F-statistic suggest that the ARIMA (1,0,0)(1,0,0) model was correctly specified.

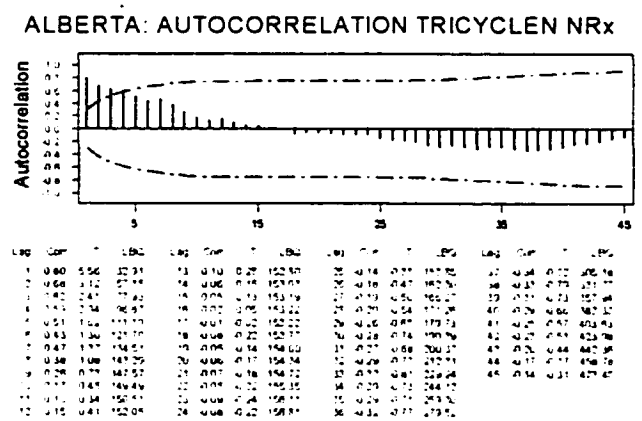
**Figure 4.7: Tricyclen Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta**



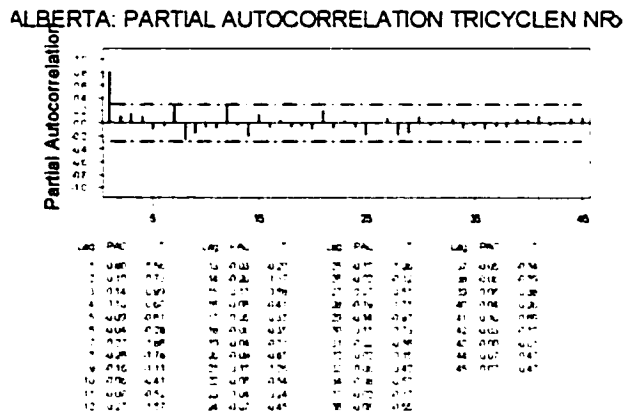



**Table 4.5: Tri-cyclen Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta ARIMA (1,0,0)(1,0,0) Model**

| | Ontario | | | | | Quebec | | | | | Alberta | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob |
| 1 | 0.038 | 0.038 | 0.0540 | | 1 | -0.172 | -0.172 | 1.0966 | | 1 | -0.098 | -0.098 | 0.3596 | |
| 2 | 0.031 | 0.029 | 0.0901 | | 2 | -0.153 | -0.188 | 1.9877 | | 2 | 0.135 | 0.127 | 1.0589 | |
| 3 | -0.257 | -0.260 | 2.6977 | 0.100 | 3 | 0.174 | 0.118 | 3.1874 | 0.074 | 3 | -0.188 | -0.168 | 2.4499 | 0.118 |
| 4 | -0.030 | -0.011 | 2.7352 | 0.255 | 4 | -0.207 | -0.195 | 4.9340 | 0.085 | 4 | 0.004 | -0.043 | 2.4504 | 0.294 |
| 5 | -0.086 | -0.072 | 3.0510 | 0.384 | 5 | -0.028 | -0.054 | 4.9670 | 0.174 | 5 | -0.335 | -0.311 | 7.2003 | 0.066 |
| 6 | -0.156 | -0.232 | 4.1107 | 0.391 | 6 | 0.008 | -0.101 | 4.9697 | 0.290 | 6 | -0.078 | -0.181 | 7.4690 | 0.113 |
| 7 | 0.054 | 0.069 | 4.2444 | 0.515 | 7 | -0.269 | -0.281 | 8.2533 | 0.143 | 7 | 0.163 | 0.225 | 8.6700 | 0.123 |
| 8 | -0.024 | -0.070 | 4.2709 | 0.640 | 8 | -0.007 | -0.185 | 8.2558 | 0.220 | 8 | 0.047 | 0.004 | 8.7758 | 0.187 |
| 9 | -0.051 | -0.184 | 4.3969 | 0.733 | 9 | 0.231 | 0.103 | 10.878 | 0.144 | 9 | 0.135 | 0.057 | 9.6641 | 0.208 |
| 10 | -0.118 | -0.100 | 5.1035 | 0.746 | 10 | -0.149 | -0.116 | 12.014 | 0.151 | 10 | 0.065 | 0.036 | 9.8771 | 0.274 |
| 11 | 0.176 | 0.154 | 6.7550 | 0.663 | 11 | 0.132 | 0.062 | 12.939 | 0.165 | 11 | 0.046 | -0.044 | 9.9896 | 0.351 |
| 12 | -0.118 | -0.276 | 7.5283 | 0.675 | 12 | 0.111 | 0.014 | 13.626 | 0.191 | 12 | -0.113 | 0.029 | 10.706 | 0.381 |
| 13 | 0.026 | -0.028 | 7.5684 | 0.751 | 13 | -0.082 | 0.019 | 14.018 | 0.232 | 13 | -0.074 | -0.015 | 11.026 | 0.441 |
| 14 | -0.214 | -0.183 | 10.367 | 0.584 | 14 | 0.261 | 0.216 | 18.191 | 0.110 | 14 | -0.023 | 0.017 | 11.059 | 0.524 |
| 15 | 0.132 | -0.034 | 11.494 | 0.569 | 15 | 0.013 | 0.153 | 18.203 | 0.150 | 15 | 0.063 | 0.137 | 11.313 | 0.585 |
| 16 | -0.092 | -0.180 | 12.067 | 0.601 | 16 | -0.464 | -0.337 | 32.871 | 0.003 | 16 | -0.150 | -0.225 | 12.844 | 0.539 |

**Table 4.6: Tri-cyclen – Ontario ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Ontario NRx Volume
**Method: Least Squares**
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -155.0835 | 158.5317 | -0.978249 | 0.3360 |
| **C** | 2944.938 | 1531.919 | 1.922384 | 0.0644 |
| **Lagged NRx** | 0.799828 | 0.100923 | 7.925148 | 0.0000 |
| **Autoregressive (1)** | -0.466891 | 0.165532 | -2.820542 | 0.0086 |
| **Seasonal AR(12)** | 0.489553 | 0.141559 | 3.458295 | 0.0017 |
| **R-squared** | 0.895820 | **Mean (NRx)** | | 11687.59 |
| **Adjusted R-squared** | 0.881450 | **S.D. (NRx)** | | 1676.440 |
| **Log likelihood** | -261.7192 | **F-statistic** | | 62.34083 |
| **Durbin-Watson** | 1.919446 | **P-Value** | | 0.000000 |

**Table 4.7: Tri-cyclen – Quebec ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Quebec NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 123.5310 | 89.97032 | 1.373019 | 0.1803 |
| **C** | 8663.592 | 3024.483 | 2.864487 | 0.0077 |
| **Lagged NRx** | 0.533527 | 0.150846 | 3.536891 | 0.0014 |
| **Autoregressive (1)** | -0.462070 | 0.187774 | -2.460781 | 0.0201 |
| **Seasonal AR(12)** | 0.728744 | 0.044259 | 16.46559 | 0.0000 |
| **R-squared** | 0.961419 | **Mean (NRx)** | | 12912.97 |
| **Adjusted R-squared** | 0.956098 | **S.D. (NRx)** | | 1611.845 |
| **Log likelihood** | -243.4960 | **F-statistic** | | 180.6673 |
| **Durbin-Watson** | 2.255502 | **P-Value** | | 0.000000 |

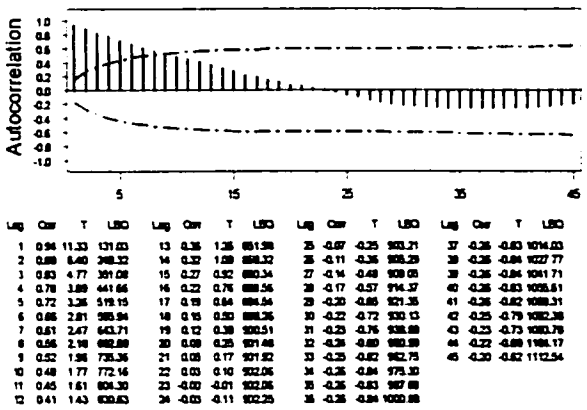
**Table 4.8: Tri-cyclen – Alberta ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Alberta NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

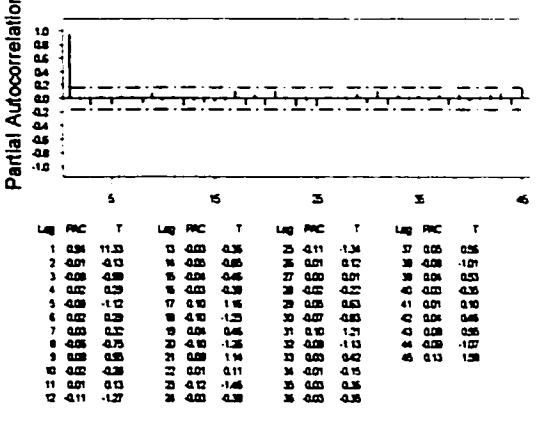
| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -101.0060 | 185.4209 | -0.544739 | 0.5901 |
| **C** | 3141.542 | 2131.226 | 1.474054 | 0.1512 |
| **Lagged NRx** | 0.424943 | 0.387942 | 1.095376 | 0.2824 |
| **Autoregressive (1)** | -0.025239 | 0.400824 | -0.062968 | 0.9502 |
| **Seasonal AR(12)** | 0.337690 | 0.114992 | 2.936647 | 0.0064 |
| **R-squared** | 0.488734 | **Mean (NRx)** | | 5011.882 |
| **Adjusted R-squared** | 0.418214 | **S.D. (NRx)** | | 548.5649 |
| **Log likelihood** | -250.7801 | **F-statistic** | | 6.930480 |
| **Durbin-Watson** | 2.136817 | **P-Value** | | 0.000482 |

**Figure 4.8: Triphasil Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta**

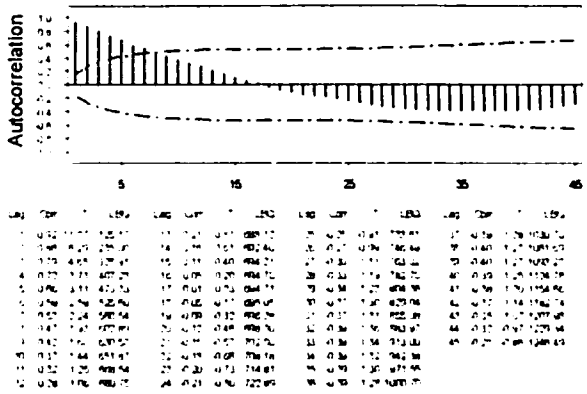
ONTARIO: AUTOCORRELATION TRIPHASIL NRx



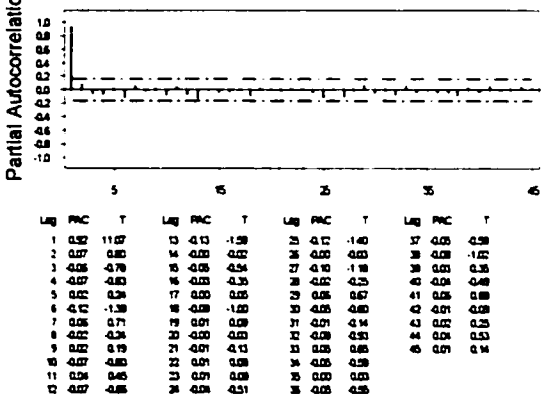

ONTARIO: PARTIAL AUTOCORRELATION TRIPHASIL NRx



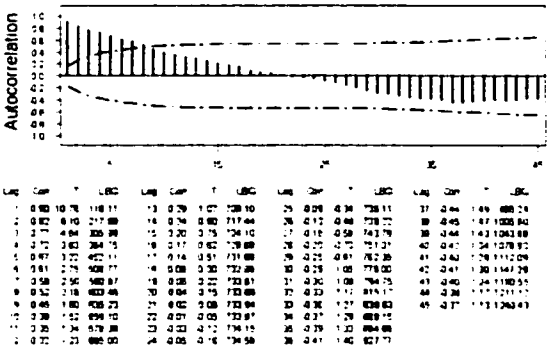

QUEBEC: AUTOCORRELATION TRIPHASIL NRx




QUEBEC: PARTIAL AUTOCORRELATION TRIPHASIL NRx




ALBERTA: AUTOCORRELATION TRIPHASIL NRx




ALBERTA: PARTIAL AUTOCORRELATION TRIPHASIL NRx

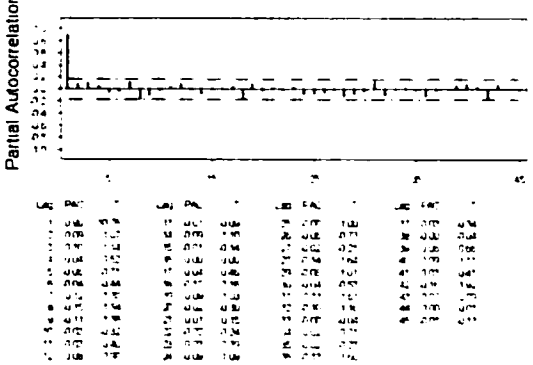


**Table 4.9: Triphasil Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta ARIMA (1,0,0)(1,0,0) Model**

| | Ontario | | | | | Quebec | | | | | Alberta | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob |
| 1 | 0.065 | 0.065 | 0.1574 | | 1 | -0.105 | -0.105 | 0.4078 | | 1 | -0.198 | -0.198 | 1.4511 | |
| 2 | 0.001 | -0.003 | 0.1574 | | 2 | -0.040 | -0.051 | 0.4681 | | 2 | -0.039 | -0.082 | 1.5108 | |
| 3 | 0.100 | 0.100 | 0.5493 | 0.459 | 3 | 0.100 | 0.092 | 0.8649 | 0.352 | 3 | 0.034 | 0.009 | 1.5555 | 0.212 |
| 4 | -0.134 | -0.149 | 1.2807 | 0.527 | 4 | -0.150 | -0.134 | 1.7835 | 0.410 | 4 | 0.135 | 0.147 | 2.2955 | 0.317 |
| 5 | -0.208 | -0.194 | 3.1080 | 0.375 | 5 | 0.011 | -0.010 | 1.7887 | 0.617 | 5 | -0.313 | -0.268 | 6.4189 | 0.093 |
| 6 | -0.273 | -0.280 | 6.3778 | 0.173 | 6 | -0.018 | -0.039 | 1.8024 | 0.772 | 6 | -0.103 | -0.231 | 6.8811 | 0.142 |
| 7 | 0.186 | 0.269 | 7.9484 | 0.159 | 7 | -0.075 | -0.057 | 2.0560 | 0.841 | 7 | 0.129 | 0.035 | 7.6338 | 0.178 |
| 8 | 0.135 | 0.177 | 8.8092 | 0.185 | 8 | -0.035 | -0.073 | 2.1144 | 0.909 | 8 | -0.043 | -0.012 | 7.7210 | 0.259 |
| 9 | 0.020 | 0.026 | 8.8293 | 0.265 | 9 | 0.368 | 0.375 | 8.7473 | 0.271 | 9 | 0.003 | 0.087 | 7.7216 | 0.358 |
| 10 | 0.122 | -0.090 | 9.5940 | 0.295 | 10 | -0.216 | -0.190 | 11.128 | 0.195 | 10 | 0.017 | -0.036 | 7.7371 | 0.460 |
| 11 | 0.166 | 0.081 | 11.059 | 0.272 | 11 | 0.101 | 0.129 | 11.666 | 0.233 | 11 | -0.004 | -0.151 | 7.7381 | 0.561 |
| 12 | -0.002 | 0.048 | 11.059 | 0.353 | 12 | 0.031 | -0.081 | 11.718 | 0.304 | 12 | -0.006 | -0.006 | 7.7401 | 0.654 |
| 13 | -0.013 | 0.202 | 11.070 | 0.437 | 13 | -0.168 | -0.014 | 13.361 | 0.270 | 13 | -0.009 | 0.003 | 7.7444 | 0.736 |
| 14 | -0.062 | -0.086 | 11.302 | 0.503 | 14 | 0.042 | -0.094 | 13.471 | 0.336 | 14 | -0.083 | -0.080 | 8.1613 | 0.772 |
| 15 | 0.021 | -0.008 | 11.329 | 0.583 | 15 | -0.179 | -0.126 | 15.538 | 0.275 | 15 | 0.114 | 0.120 | 8.9923 | 0.774 |
| 16 | -0.146 | -0.193 | 12.777 | 0.544 | 16 | 0.133 | 0.187 | 16.743 | 0.270 | 16 | -0.018 | -0.037 | 9.0134 | 0.830 |

**Table 4.10: Triphasil – Ontario ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Ontario NRx Volume
**Method: Least Squares**
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -166.3899 | 161.0526 | -1.033140 | 0.3101 |
| **C** | 611.1541 | 696.2183 | 0.877820 | 0.3873 |
| **Lagged NRx** | 0.927415 | 0.082487 | 11.24311 | 0.0000 |
| **Autoregressive (1)** | -0.298095 | 0.183768 | -1.622131 | 0.1156 |
| **Seasonal AR(12)** | -0.113369 | 0.187301 | -0.605279 | 0.5497 |
| **R-squared** | 0.714969 | **Mean (NRx)** | | 8287.676 |
| **Adjusted R-squared** | 0.675654 | **S.D. (NRx)** | | 753.0690 |
| **Log likelihood** | -251.6201 | **F-statistic** | | 18.18583 |
| **Durbin-Watson** | 1.724517 | **P-Value** | | 0.000000 |

**Table 4.11: Triphasil – Quebec ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Quebec NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

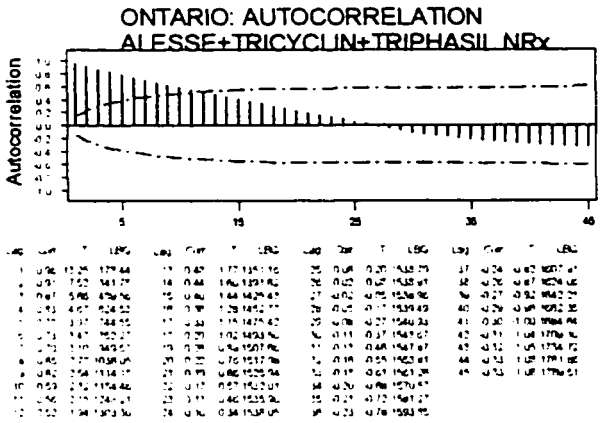
| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 232.5364 | 98.90275 | 2.351162 | 0.0257 |
| **C** | 2670.089 | 1833.244 | 1.456483 | 0.1560 |
| **Lagged NRx** | 0.623403 | 0.131332 | 4.746774 | 0.0001 |
| **Autoregressive (1)** | -0.507240 | 0.178679 | -2.838832 | 0.0082 |
| **Seasonal AR(12)** | 0.848687 | 0.067453 | 12.58191 | 0.0000 |
| **R-squared** | 0.931344 | **Mean (NRx)** | | 15395.06 |
| **Adjusted R-squared** | 0.921874 | **S.D. (NRx)** | | 1331.590 |
| **Log likelihood** | -246.7998 | **F-statistic** | | 98.34919 |
| **Durbin-Watson** | 2.141223 | **P-Value** | | 0.000000 |

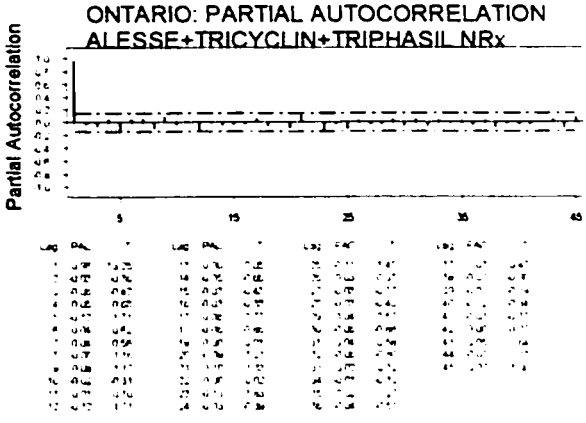
**Table 4.12: Triphasil – Alberta ARIMA (1,0,0)(1,0,0) Model**

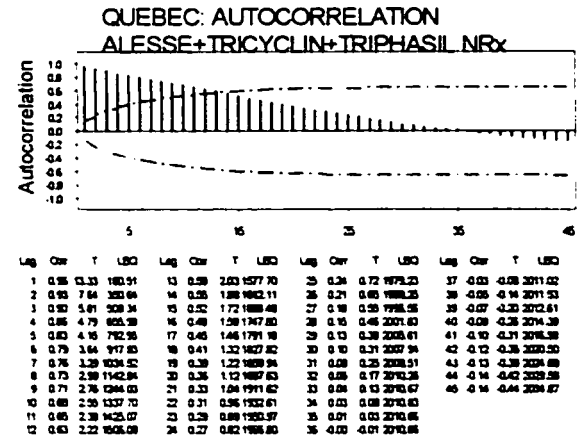
**Dependent Variable:** Alberta NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

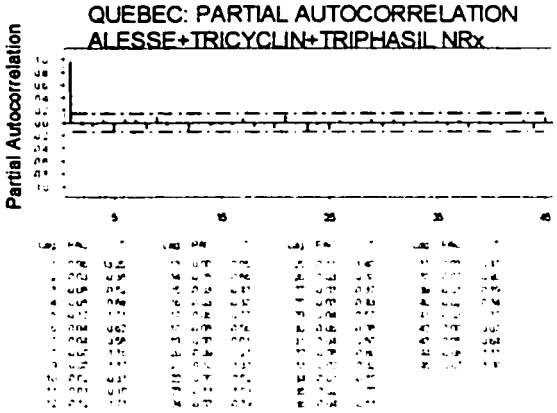
| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -29.39871 | 134.3045 | -0.218896 | 0.8283 |
| **C** | 418.3682 | 273.6201 | 1.529011 | 0.1371 |
| **Lagged NRx** | 0.865671 | 0.075163 | 11.51730 | 0.0000 |
| **Autoregressive (1)** | -0.346563 | 0.133531 | -2.595381 | 0.0147 |
| **Seasonal AR(12)** | 0.041124 | 0.095732 | 0.429577 | 0.6707 |
| **R-squared** | 0.739840 | **Mean (NRx)** | | 3499.176 |
| **Adjusted R-squared** | 0.703956 | **S.D. (NRx)** | | 697.6851 |
| **Log likelihood** | -247.4707 | **F-statistic** | | 20.61749 |
| **Durbin-Watson** | 2.355468 | **P-Value** | | 0.000000 |

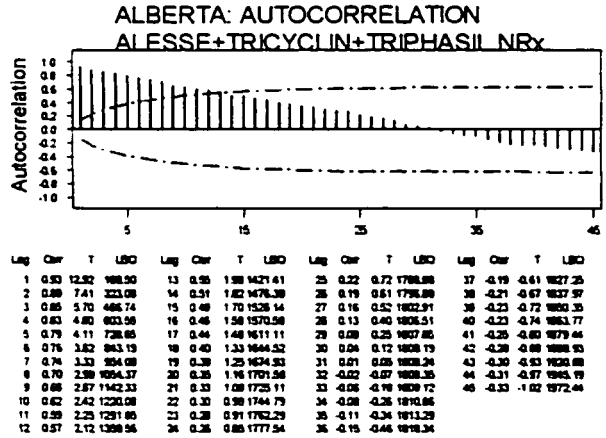
**Figure 4.9: Alesse+Tri-cyclen+Triphasil Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta**



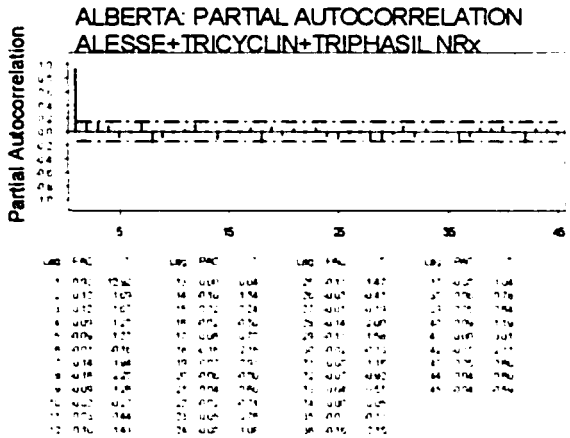



**Table 4.13: Alesse+Tri-cyclen+Triphasil Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta ARIMA (1,0,0)(1,0,0) Model**

| | Ontario | | | | | Quebec | | | | | Alberta | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob |
| 1 | 0.020 | 0.020 | 0.0146 | | 1 | -0.069 | -0.069 | 0.1785 | | 1 | -0.099 | -0.099 | 0.3652 | |
| 2 | -0.043 | -0.043 | 0.0853 | | 2 | -0.140 | -0.146 | 0.9297 | | 2 | 0.141 | 0.133 | 1.1283 | |
| 3 | -0.094 | -0.092 | 0.4338 | 0.510 | 3 | 0.075 | 0.055 | 1.1521 | 0.283 | 3 | -0.091 | -0.067 | 1.4523 | 0.228 |
| 4 | -0.130 | -0.130 | 1.1208 | 0.571 | 4 | -0.179 | -0.195 | 2.4581 | 0.293 | 4 | 0.092 | 0.062 | 1.7977 | 0.407 |
| 5 | -0.148 | -0.158 | 2.0515 | 0.562 | 5 | -0.123 | -0.138 | 3.0952 | 0.377 | 5 | -0.285 | -0.262 | 5.2287 | 0.156 |
| 6 | -0.277 | -0.315 | 5.4011 | 0.249 | 6 | -0.023 | -0.112 | 3.1180 | 0.538 | 6 | -0.139 | -0.222 | 6.0702 | 0.194 |
| 7 | 0.075 | 0.013 | 5.6595 | 0.341 | 7 | -0.126 | -0.176 | 3.8322 | 0.574 | 7 | 0.138 | 0.211 | 6.9311 | 0.226 |
| 8 | 0.024 | -0.077 | 5.6866 | 0.459 | 8 | 0.105 | 0.030 | 4.3490 | 0.630 | 8 | 0.011 | 0.054 | 6.9368 | 0.327 |
| 9 | 0.046 | -0.066 | 5.7896 | 0.565 | 9 | 0.245 | 0.183 | 7.2958 | 0.399 | 9 | 0.064 | 0.048 | 7.1391 | 0.415 |
| 10 | 0.098 | -0.004 | 6.2770 | 0.616 | 10 | -0.217 | -0.213 | 9.6908 | 0.287 | 10 | 0.086 | 0.066 | 7.5177 | 0.482 |
| 11 | 0.178 | 0.114 | 7.9614 | 0.538 | 11 | 0.130 | 0.109 | 10.588 | 0.305 | 11 | 0.072 | -0.073 | 7.7912 | 0.555 |
| 12 | -0.065 | -0.142 | 8.1981 | 0.609 | 12 | -0.003 | -0.096 | 10.589 | 0.390 | 12 | -0.020 | 0.035 | 7.8124 | 0.647 |
| 13 | -0.094 | -0.049 | 8.7180 | 0.648 | 13 | -0.125 | -0.004 | 11.493 | 0.403 | 13 | -0.046 | 0.031 | 7.9384 | 0.719 |
| 14 | -0.140 | -0.155 | 9.9107 | 0.624 | 14 | 0.098 | 0.066 | 12.083 | 0.439 | 14 | -0.053 | -0.073 | 8.1086 | 0.777 |
| 15 | 0.083 | 0.111 | 10.351 | 0.665 | 15 | -0.132 | -0.137 | 13.199 | 0.433 | 15 | -0.011 | 0.053 | 8.1161 | 0.836 |
| 16 | -0.143 | -0.174 | 11.747 | 0.627 | 16 | -0.241 | -0.249 | 17.145 | 0.249 | 16 | -0.114 | -0.112 | 9.0026 | 0.831 |

**Table 4.14: Alesse+Tri-cyclen+Triphasil – Ontario ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Ontario NRx Volume
**Method: Least Squares**
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -667.1067 | 385.6236 | -1.729943 | 0.0943 |
| **C** | 5583.046 | 2684.775 | 2.079521 | 0.0465 |
| **Lagged NRx** | 0.823889 | 0.087327 | 9.434483 | 0.0000 |
| **Autoregressive (1)** | -0.415119 | 0.171233 | -2.424298 | 0.0218 |
| **Seasonal AR(12)** | 0.306206 | 0.174698 | 1.752779 | 0.0902 |
| **R-squared** | 0.832553 | **Mean (NRx)** | | 27793.62 |
| **Adjusted R-squared** | 0.809456 | **S.D. (NRx)** | | 2922.812 |
| **Log likelihood** | -288.6862 | **F-statistic** | | 36.04719 |
| **Durbin-Watson** | 1.952638 | **P-Value** | | 0.000000 |

**Table 4.15: Alesse+Tri-cyclen+Triphasil – Quebec ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Quebec NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 544.4398 | 246.0331 | 2.212872 | 0.0349 |
| **C** | 40977.88 | 13756.42 | 2.978818 | 0.0058 |
| **Lagged NRx** | 0.256772 | 0.245446 | 1.046146 | 0.3041 |
| **Autoregressive (1)** | -0.431287 | 0.248066 | -1.738597 | 0.0927 |
| **Seasonal AR(12)** | 0.786867 | 0.031695 | 24.82649 | 0.0000 |
| **R-squared** | 0.954003 | **Mean (NRx)** | | 39989.82 |
| **Adjusted R-squared** | 0.947659 | **S.D. (NRx)** | | 3570.593 |
| **Log likelihood** | -273.5269 | **F-statistic** | | 150.3694 |
| **Durbin-Watson** | 2.137242 | **P-Value** | | 0.000000 |

**Table 4.16: Alesse+Tri-cyclen+Triphasil – Alberta ARIMA (1,0,0)(1,0,0) Model**

**Dependent Variable:** Alberta NRx Volume
**Method:** Least Squares
**Sample:** 1998:02 2001:12

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -381.8731 | 422.0527 | -0.904800 | 0.3730 |
| **C** | 5797.821 | 2975.188 | 1.948724 | 0.0611 |
| **Lagged NRx** | 0.502163 | 0.255572 | 1.964858 | 0.0591 |
| **Autoregressive (1)** | -0.206208 | 0.245431 | -0.840189 | 0.4077 |
| **Seasonal AR(12)** | 0.105967 | 0.130240 | 0.813622 | 0.4225 |
| **R-squared** | 0.187990 | **Mean (NRx)** | | 11373.97 |
| **Adjusted R-squared** | 0.075989 | **S.D. (NRx)** | | 950.7021 |
| **Log likelihood** | -277.3411 | **F-statistic** | | 1.678466 |
| **Durbin-Watson** | 2.125249 | **P-Value** | | 0.181913 |

Results of the ARIMA time-series intervention analysis for the two leading competitors of Alesse individually, and the combined series of all three products, suggest that DTCA used in support of Alesse may have had a positive impact on new prescriptions for competing medications in the prescription oral contraceptive market.

More specifically, while results (tables 4.5 to 4.16) indicate that the DTC coefficient in the equation NRx = DTC + C + NRx(-1) + AR(1) + SAR(12) is not significant for Tri-cyclen in any of the provinces studied, the DTC coefficient is significant for Triphasil in Quebec (DTC = 232.5, p-value 0.0257), and for the combined series (DTC = 544.4, p-value 0.0349) in Quebec.

## 4.3 Other Examples of Canadian DTCA Campaigns

While the example of Alesse was the most applicable to time-series intervention analysis according to Basara's (1996) criteria, DTCA has also been used extensively in support of two other commonly prescribed medications in Canada. More specifically, DTCA has been used in support of both Zyban (smoking cessation), and Viagra (erectile dysfunction). In order to examine the effects of DTCA on these products, IMS Health Canada new prescription data was requested for the period January 1998 to December 2001.

### Viagra

IMS Health Canada new prescription data for Viagra appear in Figures 4.10 and 4.11. Initial examination of the data series' suggests an abnormal product life-cycle curve, which peaks within 2-months post-launch and slowly, erodes to relative stability at 6-months post launch. The fact that there was a large amount of pre-launch anticipation fueled in part by the U.S. launch of this product, resulted in a large number of

prescriptions immediately preceding the DTCA campaign. This loading of the market may have rendered the impact of the DTCA campaign too small to detect. This series of data presents a problem for intervention time-series analysis. More specifically, in order to reduce the variation of the time-series the analysis should be limited to only those data points lying outside of the initial launch peak in the series. However, according to Basara's (1996) criteria an intervention time-series analysis should include a minimum of 6-months of data pre-DTCA campaign. Restricting the data to only those points post-August 1999, and thus post peak, would reduce the amount of pre-DTCA available data to 2-months as the campaign began in October 1999. As such, intervention time-series analysis is not ideal for this series of data.

Some investigative analysis of the Viagra series was completed using interrupted time-series analysis. The results of this analysis, included in Appendix 6, suggest that the DTCA factor did not have a significant impact on new prescription volume during the period in which it was used. This finding should be interpreted with caution considering the aforementioned reasons for which interrupted time-series analysis was not an ideal method for measuring DTCA impact in this specific situation.

Another method for determining whether or not DTCA for Viagra had an impact on new prescription volume is to examine differences in market share for the brand. Market share in Figure 4.11 demonstrates that within 3-months post launch Viagra had over 90% of new prescriptions in the erectile dysfunction market clearly demonstrating that Viagra in essence became the erectile dysfunction market. Noteworthy is the fact that new

prescription volume does in fact begin to demonstrate signs of increasing near the latter half of 2001 which, is the same time when Pfizer Canada Inc. initiated testimonial DTCA featuring a well-known sports celebrity. Future research using intervention time-series analysis, and several months of data for 2002 could potentially be able to determine whether or not this increase is in fact significantly related to DTCA during this period of time.

**Figure 4.10: Viagra New Prescription Volume – Ontario, Quebec, Alberta**

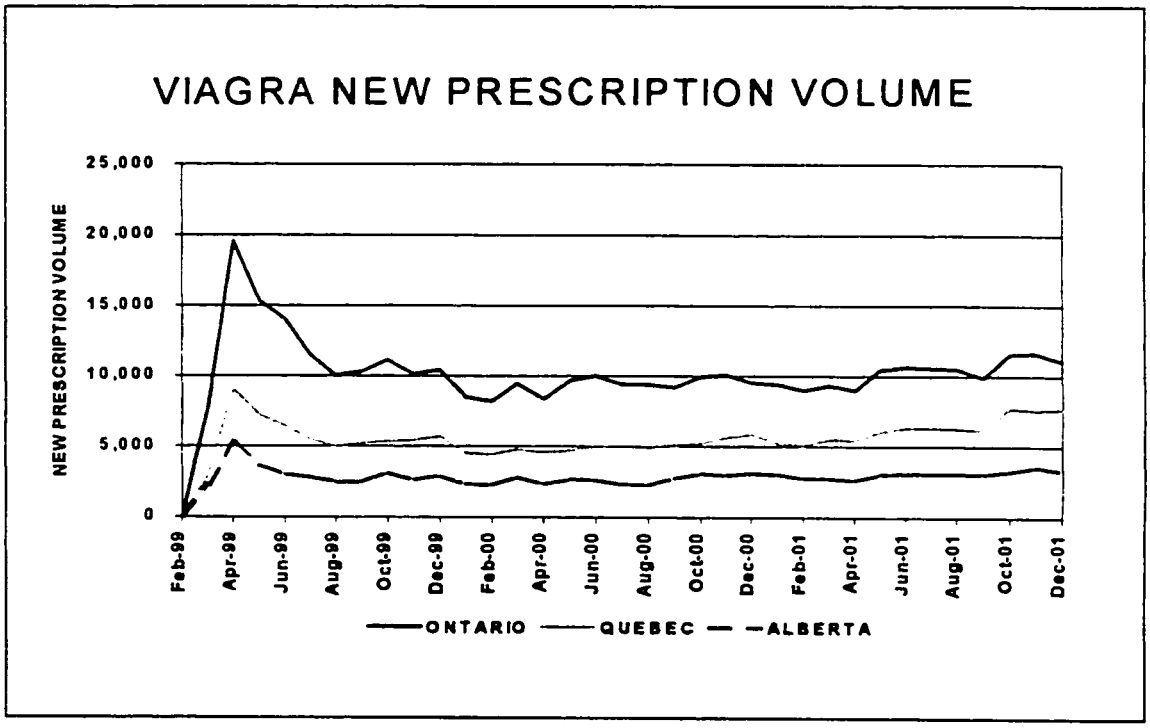
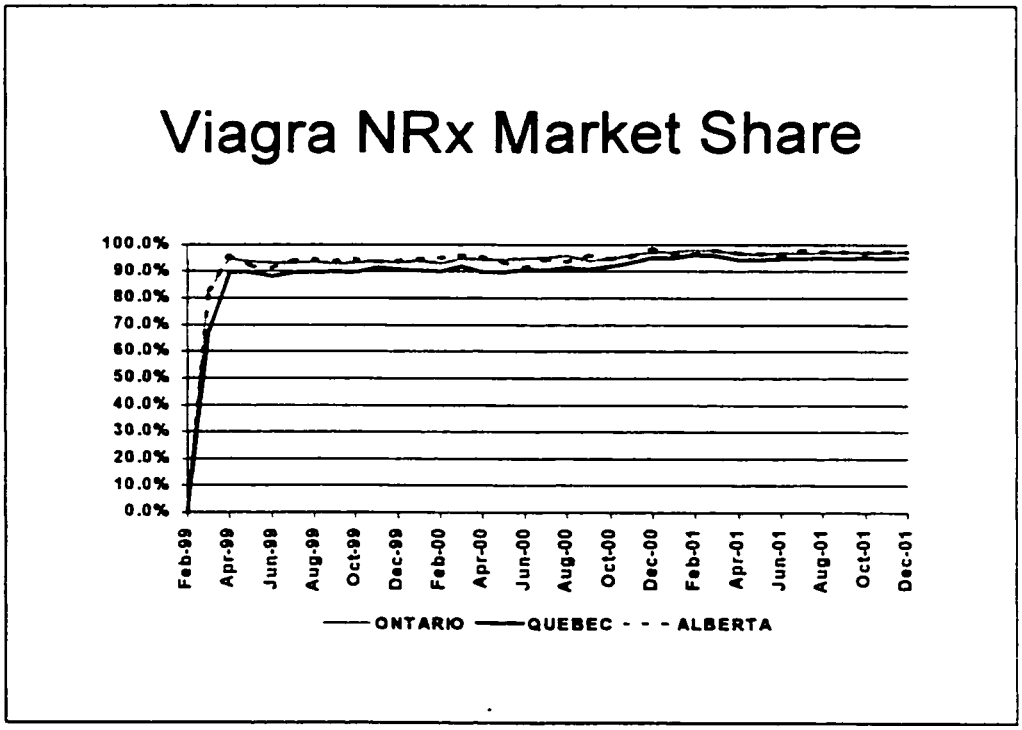


**Figure 4.11: Viagra New Prescription Share – Ontario, Quebec, Alberta**




Zyban

IMS Health Canada new prescription data for Zyban appear in Figures 4.12 and 4.13. Initial examination of the data series instantly suggests a seasonal pattern to the distribution of the series. IMS Health Canada supports this conclusion (IMS Health Canada Inc, 1999).

**Figure 4.12: Zyban New Prescription Volume – Ontario, Quebec, Alberta**

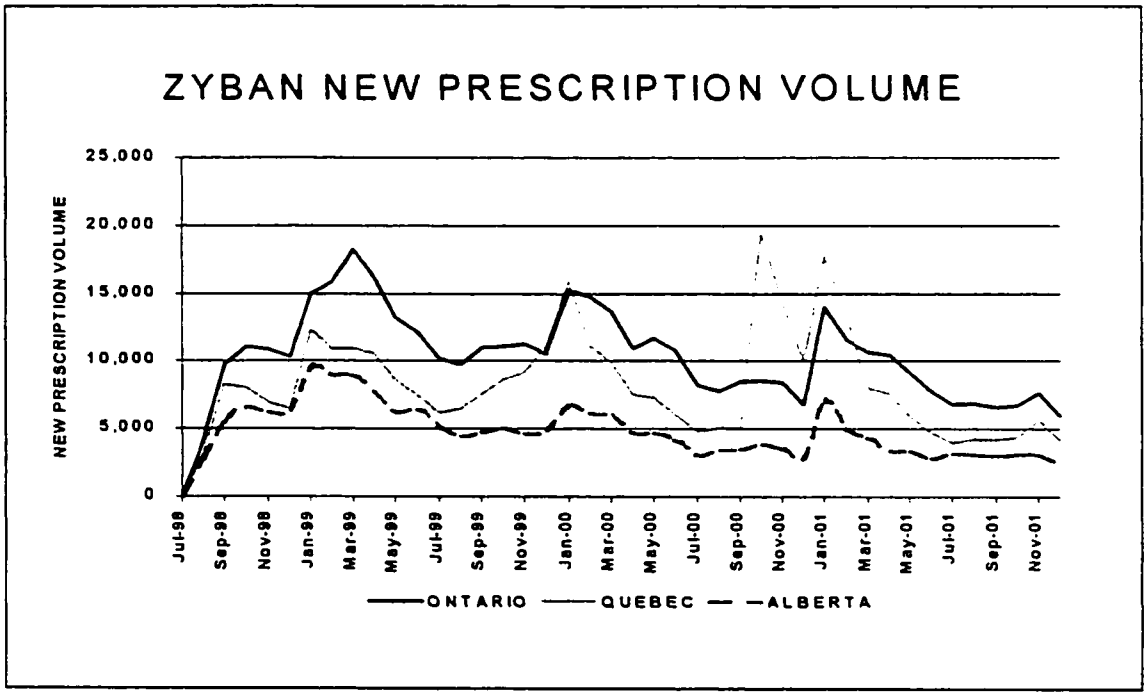
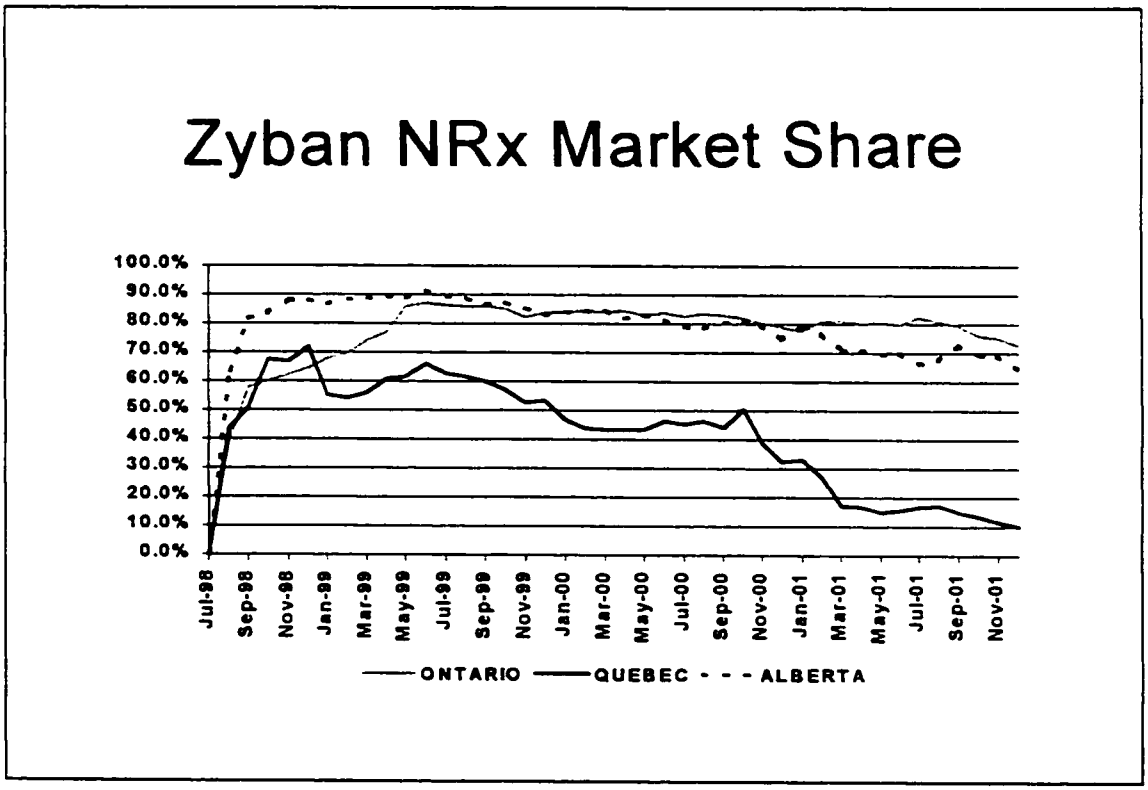



**Figure 4.13: Zyban New Prescription Share – Ontario, Quebec, Alberta**



The Zyban example is interesting as there are several confounding factors affecting the data series. To begin with the high-degree of variability of the data set, which is in part due to systematic seasonal variance, or seasonality in the market place, makes statistical analysis challenging. In order to control for the seasonality of the data set a moving average or smoothing technique can be used. Differencing of the series can control further variability of the data. The second major confounding factor is the serious health concerns surrounding the product. While GlaxoWellcome announced to Zyban users such concerns in 2001, issues with the products safety had been a concern for physicians as the U.S. FDA and Canada's Health Canada collected reports of adverse events associated with the products use. The effects of these concerns are evident in the new prescription market share for the product in Figure 4.13, which declined for each month after the products peak 6-months post-launch. The third and final confounding factor for Zyban was the listing of a major competitor on the Quebec public formulary in October 2000, which caused a major decrease in Zyban's usage.

The Zyban series is not ideal for time-series intervention analysis as the data is highly seasonal with the season peak occurring precisely during the period that the DTCA was known to occur during January through March in 1999, 2000, and 2001. In addition, use of DTCA occurs during the first seasonal-peak of the data series making comparison to prior or DTCA-free seasonal peaks impossible.

While not ideal some investigative analysis of the Zyban series was completed using interrupted time-series analysis. The analysis made use of data from July 1998 to October

2000 to remove the confounding effect of the Quebec formulary listing. The analysis included DTCA variables for the 2 periods during which DTCA took place, which happened to be the 1999 and 2000 seasonal peaks. The results of this analysis, included in Appendix 7, suggest that the DTCA factor could potentially have had a significant impact on new prescription volume during the period in which it was used. This finding should be interpreted with a high degree of caution however as the value attributed to the DTCA factor cannot be separated from the natural seasonal peak in the data series using interrupted time-series analysis. More specifically, while this method does allow the user to account for seasonal variations in data series, it is not able to isolate the impact of a variable such as DTCA without some indicator of seasonal prescription volumes without the presence of DTCA. Overall, the investigation concludes that interrupted time-series analysis was not an ideal method for measuring DTCA impact in this specific situation.

As in the Viagra example, another method for gaining insight into whether or not DTCA for Zyban had an impact on new prescription volume is to examine differences in market share for the brand. Market share in Figure 4.13 demonstrates that Zyban had very rapid uptake in each of the major markets with over 70% market share within the first 3-months of availability. Noteworthy is the fact that new prescription share peaks quickly and begins to decline. Examining the Zyban new prescription volume and share is inconclusive in terms of whether or not DTCA initiatives for Zyban had a significant impact on new prescription volume or share.

# CHAPTER 5

# DISCUSSION

## 5.1 Discussion of Findings

This research thesis includes a review and critical synthesis of literature relevant to promotional response modeling and pharmaceutical direct-to-consumer advertising (DTCA). Through an empirical investigation of the impact of direct-to-consumer advertising of a prescription medication in Canada, this research contributes to the overall knowledge of promotional response modeling in a new and under-studied market. In addition, this research presents insight into the impact of DTCA of prescription medications worthy of consideration by academics, industry professionals, and other key stakeholders.

The results of this investigation into the impact of DTCA on prescription volume in Canada are unexpected in that the null-hypothesis was rejected.

$H_1$: The number of new prescriptions for a prescription medication will increase significantly after consumers are exposed to a DTCA campaign for the medication.

The second hypothesis relating to regional differences could not be tested and thus not supported.

$H_2$: The change in number of new prescriptions for a prescription medication resulting from the exposure of consumers to a DTCA campaign will vary significantly according to regional differences.

Failure to replicate Basara's (1996) findings, while unexpected, is not surprising within the context of the Canadian pharmaceutical market. More specifically, the fact that Basara's (1996) criteria for a DTCA campaign applicable to intervention time-series analysis could not be replicated indicated that there might be some difficulty replicating previous findings in this area. Recall, in the Basara (1996) research a product for which there was no promoted competitors, and relatively ineffective competition, was used for the purpose of the analysis. In the Canadian market, none of the DTCA campaigns on record met these criteria completely.

The fact that a DTCA campaign matching the one used in the Basara (1996) research could not be identified raises some concern as to the possibility of replicating these findings in the current pharmaceutical market environment. More specifically, there are no examples of DTCA fitting Basara's (1996) criteria perfectly in the Canadian context, and likely few if any in the U.S. market context. Moreover, even the product used in the Basara (1996) research did not match these criteria precisely. This reality suggests a need to revise these criteria, and potentially the methodology used to assess impact. The primary problem lies in the considerable investment required to support a DTCA campaign.

With such high costs associated with this method of promotion, only those products for which a considerable sales volume and market share are anticipated, such as those considered blockbusters, have been promoted with this kind of communication method This is particularly true in the Canadian context. When considering blockbuster products such as these the isolation of the impact of one element of the marketing mix becomes quite challenging, as the total investment in all elements of the marketing mix is relatively high. This reality in the Canadian environment becomes quite clear within the body of this research, which focused on the three largest DTCA campaigns used in Canada within the 3-years prior to this research. While none of these products met Basara's (1996) criteria, none of these products could be considered non-blockbuster.

Another problem specific to the Alesse example lies in the fact that branding and other information was limited in the DTCA used. While the Alesse campaign did include some branding, advertisements included only a suggestion that consumers should ask their doctor to learn more about Alesse. For those patients or consumers not already familiar with Alesse and its use this advertising likely lacked meaning. In order for this DTCA to result in an actual prescription for the product advertised the consumer would have to first ask about the brand name, and either be a completely new patient not already using an oral contraceptive or a consumer willing to switch medications. Both patient types are not facing significant risk by waiting to ask about the product until their next regularly scheduled visit. As such, the true impact of this campaign may have been to simply raise awareness of the product name and indirectly associate it with its use via the use of the product imagery. Any changes in prescriptions for the brand would only have occurred

over the course of the year, thus diluting the DTCA impact, as patients visit their physicians, and not necessarily immediately during the course of the DTCA campaign.

Timing of anticipated response could also have impacted the results. This and Basara's research focused on the immediate impact of advertisements in terms of changes in new prescription volume. This may not have been the best measure of the impact of these advertising campaigns considering the time delay that may have been necessary for the increase in awareness resulting from the campaign to translate into increased demand and thus increased prescribing behaviour. Supporting this theory is the approach used in the treatment guidelines for many commonly found medical conditions in North America, which often follows a stepwise approach. This approach often begins first with the identification of an illness or condition requiring treatment and follows with a series of treatment options depending on a variety of patient and condition related factors.

DTCA in the cases of Zyban, Viagra, and Alesse, advertisements focused first on the need for patients to consult their physicians for the conditions these products treat, and second on the fact that treatments exist. One would assume that those patients with a specific need for such treatments would have already consulted their physicians when these products became available. This is particularly true for Zyban and Viagra which had such rapid uptake in their first 3-months of availability. As such, new patients consulting their physicians as a result of an unbranded informational advertisement are likely true new patients not having established a prior history of consultation. In following a standard treatment algorithm for these patients, physicians would likely follow a stepwise

approach consisting of (1) identification of disease or condition requiring treatment, (2) recommendation of treatment, (3) assessment of treatment efficacy, (4) recommendation of 2nd line treatment, and so on. In many cases, first-line treatment is not pharmacological.

In the case of Zyban first-line treatment for smoking cessation could potentially take the form of a psychological, or support-group approach. This method could be used alone, or in combination with traditional nicotine-replacement therapy prior to the identification of a need for pharmacological treatment with a product such as Zyban.

In the case of Viagra, erectile dysfunction may be related to psychological or physiological causes. However, the identification of such causes is often a time-consuming and complicated process in which several possible causes must be ruled out.

In the case of Alesse, the use of an oral contraceptive may not be the optimal solution for a patient seeking birth control. The decision to prescribe an oral medication may be dependent on a variety of factors.

In each of these cases it is clear that for true new patients there are several factors that must be considered prior to the use of prescription medications. The identification and assessment of these factors could take anywhere from a few weeks, to several months depending on the severity of the condition, the physician's own personal treatment style,

and published guidelines on the treatment approach. As such, timing of DTCA impact should be investigated further.

Results of this investigation and attempt at replication suggest the need to revisit the appropriateness of Basara's (1996) approach to measuring the impact of DTCA in the Canadian pharmaceutical market. While Basara (1996) clearly mentioned several product specific criteria that should be considered prior to using this method to assess the impact of DTCA on prescription volume, these criteria should be revisited based on the reality faced in the Canadian context. More specifically, during the past 3-years major DTCA campaigns have been used for several products in Canada. Many of these products can be considered as blockbusters and have redefined the markets in which they compete. Due to their high sales potentials, pharmaceutical manufacturers marketing these products invest heavily in a wide variety of marketing initiatives. As such, isolation of the impact of one element in the marketing mix such as DTCA is extremely difficult due to the high level of surrounding marketing noise.

While not a primary objective of this research thesis, additional analysis of the prescription data in the oral contraceptive market did reveal some interesting findings. Specifically, the DTCA coefficient was positive for one of the products competing with Alesse in one of the provinces studied. Furthermore, the DTCA coefficient was also positive for the combined total volume of prescriptions represented by summing together Alesse and its three largest competitors in one of the provinces studied. These findings are significant and suggest the possibility that DTCA in support of a pharmaceutical

medication may positively impact prescriptions for other competing products with large market shares.

## 5.2 Implications

These results of this investigation have clear implications for Canadian pharmaceutical manufacturers, government, insurers, consumer groups, and the medical community. Furthermore, these findings have important implications for those interested in furthering the overall understanding of the impact of DTCA via future research in this area.

### 5.2.1 Pharmaceutical Manufacturers

Canadian pharmaceutical manufacturers considering investing in DTCA to support the growth of certain prescription medications should carefully consider the objectives of DTCA initiatives. Assuming that the existing regulations governing the use of DTCA in Canada will not change, pharmaceutical marketers should consider both short- and long-term objectives of unbranded DTCA. Short-term objectives could include increasing awareness of a condition or illness. A longer-term objective could be to increase patient consulting for a condition or illness with the eventual objective of increasing the overall number of prescriptions for a given product. In both cases the success or failure of the DTCA campaign in terms of immediate increase or decrease of new prescription volume will be difficult to measure, and should not be a primary objective for the campaign. In

fact, despite limitations, results of this research suggest that DTCA may not have a significant impact on prescription medications for which a large investment in other methods of promotion is being used. And thus, the use of DTCA should be carefully considered in light of the substantial costs associated with it.

Canadian pharmaceutical manufacturers may also seek out ways to optimize the effectiveness of DTCA initiatives by working with Canadian physicians that are most likely to be asked about a given product or condition being advertised via DTCA. Such programs would increase the likelihood that patient inquiries are well received by physicians, and are responded to in a fashion that best meets the needs of the patient or consumer.

Pharmaceutical manufacturers may consider these findings when discussing the possibility of further revising existing legislation governing the use of DTCA in Canada with policy makers. Specifically, these findings suggest that there is an important need to revisit the issue of DTCA to ensure that information presented in DTCA is enough for patients to make informed decisions.

Finally, pharmaceutical manufacturers should consider the possible positive and negative outcomes associated with DTCA of prescription medications particularly in the competitive environment. Time-series analysis of prescription data for competing products to Alesse suggested a significant positive impact of Alesse DTCA on prescription volumes in one of the provinces studied. This finding suggests that DTCA in

a given pharmaceutical product category may favour those products with the highest market shares. In light of this, pharmaceutical manufacturers may wish to reserve investment in DTCA for those products for which a dominant market share has been achieved.

### 5.2.2 Canadian Government

This research has implications for the Canadian government. Results of this analysis do not demonstrate a relationship between DTCA and new prescription volume. The lack of a relationship in this situation could be cause for concern and begs the question of why. A potential cause for the lack of impact could be the ineffectiveness of existing DTCA campaigns to raise awareness of medical conditions and the availability of treatments for them. In contrast, there is a possibility that consumers exposed to the information contained in DTCA initiatives either do not raise this information with their physicians, or when this information is raised it is not translated into a prescription for the medication being advertised by the physician. Operating within the rules and regulations set in 1978, Canadian pharmaceutical marketers are attempting to make effective use of DTCA by presenting potentially confusing information to consumers regarding healthcare issues. In the worst-case scenarios this kind of confusion could lead to unnecessary physician visits, patient demands, and prescribing. Health Canada should consider clarifying DTCA regulations to ensure that DTCA initiatives consider the best interests of the consumer.

### 5.2.3 Consumer Groups

Consumer groups should have an interest in the findings of this research. As consumers generally become more informed with respect to issues involving healthcare via sources including the internet, media, and U.S. based advertising, the demand for unbiased Canadian information will likely increase. Consumer groups will be one of the sources of information that consumers will turn to, particularly in the absence of Canadian DTCA campaigns that provide enough information to make informed decisions. As such, considering that the examples of DTCA in this research did not demonstrate an impact on new prescription volume, it is possible that consumers are not being presented with enough information to take the steps necessary to obtain a prescription for a medication being advertised. Consumer groups may be turned to as a source of this information in the near future.

### 5.2.4 The Medical Community

This research provides important information for the Canadian medical community. While the campaigns studied did not demonstrate a significant impact in new prescription volume during the time that consumers were being exposed, it may or may not have had a longer-term impact by influencing consumer's to request more information about these products. This could have influenced overall awareness and familiarity with important treatment alternatives for important conditions in Canada. The medical community should encourage future government and industry sponsored research into both the impact

of DTCA, as well as the potential positive and negative consequence of DTCA. This research will provide key opinion leaders in the medical community with the information necessary to make recommendations regarding regulations for future DTCA that ensure that patient/consumer best interests are considered.

### 5.2.5 Market Researchers

Results of this investigation suggest that DTCA did not have an identifiable impact on new prescription volume for the products studied. These findings suggest that caution should be used when generalizing Basara's (1996) findings, particularly in the Canadian context. The impact of DTCA in this example appears to be dependent on a variety of factors including product characteristics (e.g. is this product a significant improvement over existing alternatives), market characteristics (e.g. is this market active in terms of other promoted products), and advertisement (e.g. branded versus informational), related factors. The multitude of factors potentially impacting the potential for DTCA to impact prescription volume suggests the need to examine the future use of interrupted time-series analysis for general DTCA impact assessment. In light of this consideration, other means of impact assessment should be considered.

## 5.3 Limitations

This research was designed to replicate work done by Basara (1996), which focused on the impact of DTCA in the United States. Because of the regulatory environment in

Canada the same kind of advertising has not been used. More specifically, Basara (1996) used an informational campaign, and this research used a branded campaign with no condition-related information. As there was not a perfect match, a DTCA campaign for a product that does not precisely meet the criteria recommended in the original study, was used.

Another limitation is the reliance on products experiencing relatively rapid uptake, and supported by a significant marketing investment. These products do not match the Basara (1996) example, which used a product appealing to a market, which was relatively untouched by marketing initiatives prior to its launch.

A further limitation of this research is the lack of appropriate means to measure the long-term impact of DTCA on prescription volume. While unbranded advertising designed to increase the number of patients consulting health care professionals for a given disease, illness, or condition may have been effective, the resulting increase in prescriptions could potentially occur outside of the period in which an advertising campaign is taking place

A more precise measure of DTCA volume taking place during a given month may have provided a better indication of what an actual impact should look like This research was based on known occurrences of DTCA. Unfortunately, the actual volume or value of this DTCA is not readily available. More specifically, data regarding placement and value of DTCA collected by ACNeilsen was not available. This data from ACNeilsen if

eventually obtained however would prove very useful to measure the correlation between new prescription volume and DTCA expenditure.

Another limitation of this research is the reliance on one specific type of prescription data. While new prescription volume is considered the leading indicator of prescription volume changes, and is most sensitive measure of any given event on prescribing rates, it does not permit measurement of the impact of DTCA on prescription refill rates. This limitation is particularly important for a product such as Alesse, which is used on an on-going basis by patients, thus new prescriptions account for a smaller percentage of total prescriptions. More specifically, the percentage of total prescriptions made up of new prescriptions for Alesse in Ontario in 2000 was 33% versus 63% for Zyban, which is a more acute therapy. An examination of refill rates could provide some insight into DTCA impact on brand loyalty and compliance with treatment recommendations.

Findings of the research suggest the possibility that DTCA initiatives may favour prescription medications with high market shares. This finding should be considered in light of the fact that it was isolated to one particular province. Furthermore, the significance of the DTC coefficient was not consistent for both competing products studied individually; rather it was significant for one product and for the combined new prescription volume of the three leading products in that province. In light of this, generalization of this finding should be done with caution.

A final, and significant limitation of this research is the inability to control for confounding factors such as spillover of pharmaceutical DTCA from the U.S. market, and other promotion of these products via traditional means. It is estimated that there is a considerable degree of pharmaceutical DTCA being spilled-over via the U.S. media that is commonly referred to by Canadian consumers. A large number of magazines available in Canada include U.S. advertising, as do the majority of television stations. Furthermore, specific to the case of Alesse, Ortho-Tri-Cyclen an oral contraceptive was heavily advertised using DTCA in the U.S. during 2000. In fact Ortho-Tri-Cyclen recorded the 17th largest expenditure in DTCA during 2000 at $47 million (Rosenthal et al, 2002). This heavy investment in DTCA in support of another oral contraceptive available in Canada under the name of Tri-cyclen during the same time frame as the Alesse campaign could have diluted the impact of Canadian advertising.

Clearly, there were significant limitations to this research. However, this study was conducted using the best data available, the best examples of DTCA at the time, and using the same methodology as Basara (1996).

## 5.4 Directions for Future Research

Future research may consider a delayed-response model to measure the impact of Canadian unbranded DTCA. More specifically, the outcome of unbranded DTCA could be that more new patients enter the market, and the resulting impact on prescriptions could potentially occur three or more months post-campaign.

Other more direct approaches could look to the actual number of patients consulting for an advertised condition to look for increases resulting from such advertising. Many companies using DTCA are looking to other means of measuring success including, calls to 1-800 numbers, web-site visits, and research with consumers. IMS Health Canada currently collects data relating to patient visits, and analysis of this data could be interesting.

Another area that should be explored is the potential impact of DTCA campaigns on refill and total prescriptions to assess whether or not such campaigns are having an impact on existing patients already using advertised products. If the 'framing-effect' holds true in this market, repeat purchasing effects can result an interaction between advertising and brand usage thus enhancing compliance with treatment recommendations. Results of this research would be particularly useful to all involved in pharmaceutical DTCA, and if proven could be important because of the patient related benefits.

Finally, looking to other innovative field experiments may also help shed some light on the true impact of future DTCA initiatives. Specifically, field experiments where patients are monitored over time may help to reveal behavioural changes such as information seeking or prescription demand associated with DTCA exposure.

## 5.5 Conclusion

In light of previous research in the area of promotional-response this failure to replicate past research is not surprising. Past research in the area has identified similar problems in terms of establishing models that can be generalized to other markets and products. In light of this, this research is consistent with past findings and suggests that continued need to focus on replication of past studies, and identification of new methods for measuring promotional-response.

While the results of this analysis of DTCA impact suggest the Alesse campaign had little or no impact on prescription volume, in 2001 advertisers have sustained their investment in DTCA. Examples of current DTCA include Pfizer's new investment behind cholesterol screening (Lipitor) and erectile dysfunction (Viagra), Wyeth-Ayerst's continued investment in televised DTCA for Alesse, and GlaxoWellcome's continued investment in advertising in support of Zyban. One major difference between these new campaigns and prior DTCA is a more clear and concise call-to-action, which appeals to the need for consumers to consult their physicians.

Depending on the decisions made by both the Canadian government and the pharmaceutical industry the future DTCA in Canada could change drastically in the near future. With several new blockbusters on the horizon new DTCA initiatives will undoubtedly include new communication mediums as well as more comprehensive strategies including several communication vehicles. These new approaches will

facilitate the measurement of impact and will improve the likelihood of actually having an impact on new prescription volume.

Continued research in the field of promotional-response measurement, particularly into the potential impact of DTCA on new prescription volume, is important in order to provide insight and clarification to this growing area of marketing.

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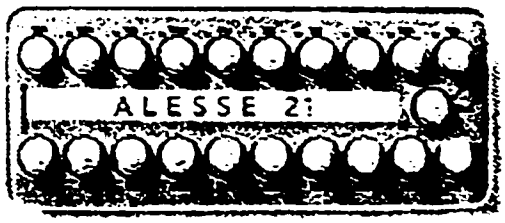
# APPENDIX 1

# SAMPLE OF ALESSE DTCA ADVERTISING

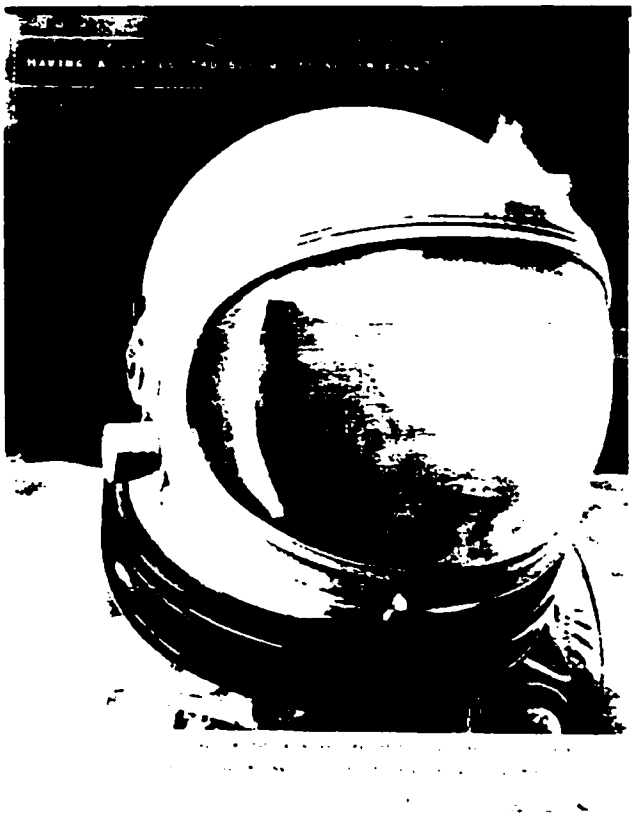



To learn more, ask your doctor

*...women, some small, such as the ones above, get Alesse birth control pills will go to air next week on MuchMusic. The women will name the drug and tell about what it does — but never do both in the same ad. They also use what appears to be carefully selected language to conform to the Act's provi-*
*sion.*

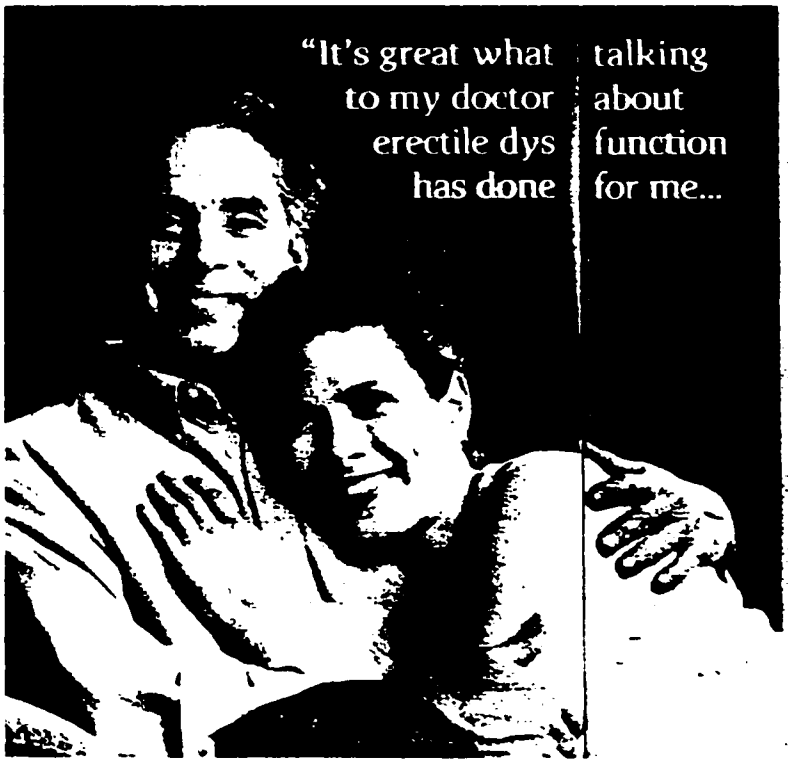
# APPENDIX 2

# SAMPLE OF ZYBAN DTCA ADVERTISING



# APPENDIX 3

# SAMPLE OF VIAGRA DTCA ADVERTISING




... but it's truly amazing what it's done for us."

"When I first started having problems, I didn't want to admit there was anything wrong. I thought that erectile dysfunction happened to other, older people. But when it started to put a real strain on our relationship, I talked to my doctor.

I learned that I was not in am alone. Over 2 million Canadian men are affected to various degrees by this condition. I also learned about the safe and effective treatment options that are available.

Sex is part of a healthy relationship, and now it is part of ours again."

*You don't have to live with the problem. Talk to your doctor now about erectile dysfunction (also known as impotence) and the options best suited to both of you. Or get the encouraging facts by calling the number below, or by visiting the informative web site.*

Call 1-800-650-1313
or visit
www.oursexualhealth.com

# APPENDIX 4

# SAMPLE OF XENICAL DTCA ADVERTISING

LOSE A *little weight* AND
PRETTY SOON YOU'LL NOTICE
HOW GREAT *you feel.*

There are **weight loss treatment options now available** to help you.
**Talk to your doctor today.**

# APPENDIX 5

# SAMPLE OF DIANE-35 DTCA ADVERTISING


Finally,
Diane
has
spots on her face she's thrilled
about...
The acne solution for women only.

# APPENDIX 6

# VIAGRA INTERVENTION TIME-SERIES ANALYSIS

In order to determine the necessary level of differencing examination of the time-series plot (Figure 3), autocorrelation (AC), and partial autocorrelation (PAC) (Figure 7) was used. Based on the fact that lag 1 was within the two standard error bounds of the PAC plot 1 level of differencing was specified.

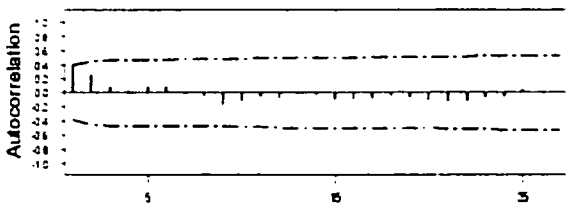
In order to determine the number of autoregressive ($p$) and moving average ($q$) parameters necessary to yield an effective model of the process several models were assessed. After considering the coefficients of determination ($R^2$), F-values, and significance levels of several alternative regression models, one with 1st level differencing (d), 1 moving average (q) parameter, 1 seasonal moving average parameter (sq), and 0 autoregressive (p) parameters was appropriate for each of the series. (p,d,q)(sp,sd,sq) = (0,1,1)(0,0,1).

NRx Volume = DTCA + C + D(NRX) + NRX(-1) + MA(1) + SMA(12)

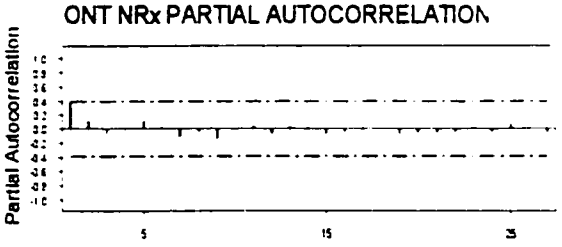
The (0,1,1)(0,0,1) model selection was justified by measuring determining that the residuals of the model were stationary and significantly different from zero using the Box-Ljung Q-statistic. Because the error series associated with the calculated ARIMA models were stationary and none of the values were significantly different from zero using the Box-Ljung Q-statistic (Table 9), and $R^2$ values were high (Tables 10-12), the ARIMA (0,1,1)(0,0,1) model was correctly specified.

# Viagra Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta

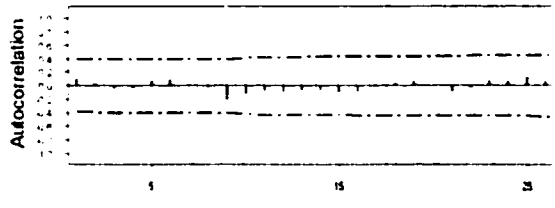
ONT NRx AUTOCORRELATION



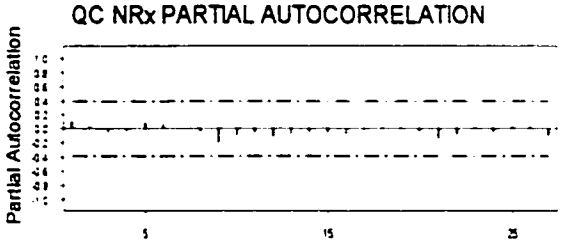

ONT NRx PARTIAL AUTOCORRELATION



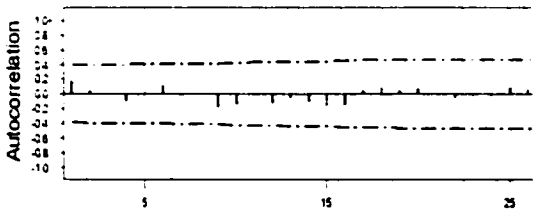

QC NRx AUTOCORRELATION



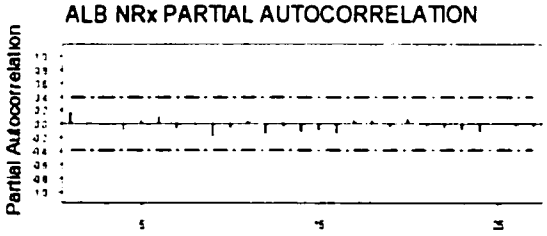

QC NRx PARTIAL AUTOCORRELATION




ALB NRx AUTOCORRELATION




ALB NRx PARTIAL AUTOCORRELATION



**Viagra Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta ARIMA (0,1,1)(0,0,1) Model**

| | Ontario | | | | | Quebec | | | | | Alberta | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob |
| 1 | -0.032 | -0.032 | 0.0281 | | 1 | -0.131 | -0.131 | 0.4651 | | 1 | -0.080 | -0.080 | 0.1729 | |
| 2 | -0.062 | -0.063 | 0.1369 | | 2 | -0.180 | -0.201 | 1.3886 | | 2 | -0.166 | -0.173 | 0.9514 | |
| 3 | -0.174 | -0.179 | 1.0394 | 0.308 | 3 | 0.137 | 0.088 | 1.9498 | 0.163 | 3 | -0.032 | -0.064 | 0.9822 | 0.322 |
| 4 | -0.421 | -0.456 | 6.5774 | 0.037 | 4 | -0.453 | -0.488 | 8.3589 | 0.015 | 4 | -0.240 | -0.290 | 2.7861 | 0.248 |
| 5 | 0.128 | 0.040 | 7.1194 | 0.068 | 5 | 0.085 | 0.027 | 8.5962 | 0.035 | 5 | 0.066 | -0.012 | 2.9276 | 0.403 |
| 6 | -0.011 | -0.128 | 7.1238 | 0.129 | 6 | 0.328 | 0.170 | 12.332 | 0.015 | 6 | 0.047 | -0.060 | 3.0048 | 0.557 |
| 7 | 0.241 | 0.111 | 9.2623 | 0.099 | 7 | -0.085 | 0.087 | 12.600 | 0.027 | 7 | 0.049 | 0.033 | 3.0940 | 0.685 |
| 8 | 0.159 | 0.026 | 10.243 | 0.115 | 8 | 0.049 | -0.092 | 12.692 | 0.048 | 8 | 0.209 | 0.175 | 4.7902 | 0.571 |
| 9 | -0.252 | -0.190 | 12.889 | 0.075 | 9 | -0.091 | -0.108 | 13.034 | 0.071 | 9 | -0.099 | -0.017 | 5.1944 | 0.636 |
| 10 | -0.035 | -0.060 | 12.945 | 0.114 | 10 | -0.126 | 0.104 | 13.736 | 0.089 | 10 | -0.259 | -0.213 | 8.1881 | 0.415 |
| 11 | -0.041 | 0.133 | 13.025 | 0.161 | 11 | 0.044 | -0.031 | 13.827 | 0.129 | 11 | 0.083 | 0.061 | 8.5177 | 0.483 |
| 12 | 0.119 | 0.143 | 13.764 | 0.184 | 12 | 0.181 | 0.170 | 15.529 | 0.114 | 12 | 0.154 | 0.195 | 9.7547 | 0.462 |
| 13 | 0.103 | -0.045 | 14.367 | 0.213 | 13 | -0.013 | -0.104 | 15.540 | 0.159 | 13 | 0.103 | 0.126 | 10.351 | 0.499 |
| 14 | -0.126 | -0.154 | 15.361 | 0.222 | 14 | -0.059 | 0.002 | 15.754 | 0.203 | 14 | -0.117 | -0.174 | 11.204 | 0.512 |
| 15 | -0.022 | -0.042 | 15.395 | 0.283 | 15 | 0.003 | 0.000 | 15.754 | 0.263 | 15 | 0.004 | 0.064 | 11.205 | 0.594 |
| 16 | -0.147 | -0.022 | 17.083 | 0.252 | 16 | -0.129 | 0.012 | 17.049 | 0.254 | 16 | -0.069 | -0.054 | 11.572 | 0.641 |
| 17 | -0.067 | -0.075 | 17.486 | 0.291 | 17 | 0.034 | -0.012 | 17.150 | 0.310 | 17 | -0.106 | -0.054 | 12.573 | 0.635 |
| 18 | 0.039 | -0.200 | 17.643 | 0.345 | 18 | 0.104 | -0.076 | 18.276 | 0.308 | 18 | 0.000 | -0.055 | 12.573 | 0.704 |
| 19 | 0.098 | -0.063 | 18.851 | 0.337 | 19 | -0.039 | 0.031 | 18.466 | 0.360 | 19 | 0.061 | -0.019 | 13.032 | 0.734 |
| 20 | 0.071 | -0.074 | 19.636 | 0.354 | 20 | -0.013 | -0.080 | 18.494 | 0.424 | 20 | 0.093 | -0.085 | 14.378 | 0.704 |

**Viagra – Ontario ARIMA (0,1,1)(0,0,1) Model**

**Dependent Variable:** Ontario NRx Volume
**Method:** Least Squares
**Sample:** 1999:07 2001:06

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -143.1232 | 738.3414 | -0.193844 | 0.8484 |
| **C** | 7461.680 | 2082.227 | 3.583510 | 0.0020 |
| **Lagged NRx** | -0.773613 | 0.217621 | -3.554873 | 0.0021 |
| **Moving Average(1)** | 0.192604 | 0.159861 | 1.204823 | 0.2431 |
| **Seasonal MA(12)** | 0.885380 | 0.000148 | 5991.856 | 0.0000 |

| | | | |
|---|---|---|---|
| **R-squared** | 0.873083 | **Mean (NRx)** | -139.2083 |
| **Adjusted R-squared** | 0.846363 | **S.D. (NRx)** | 976.6330 |
| **Log likelihood** | -173.9918 | **F-statistic** | 32.67600 |
| **Durbin-Watson stat** | 2.009723 | **P-Value** | 0.000000 |

**Viagra – Quebec ARIMA (0,1,1)(0,0,1) Model**

**Dependent Variable:** Quebec NRx Volume
**Method:** Least Squares
**Sample:** 1999:07 2001:06

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -320.5038 | 525.5272 | -0.609871 | 0.5492 |
| **C** | 3157.507 | 1493.587 | 2.114043 | 0.0480 |
| **Lagged NRx** | -0.572441 | 0.279833 | -2.045651 | 0.0549 |
| **Moving Average(1)** | 0.542629 | 0.277047 | 1.958616 | 0.0650 |
| **Seasonal MA(12)** | 0.885577 | 0.000177 | 5009.494 | 0.0000 |

| | | | |
|---|---|---|---|
| **R-squared** | 0.778976 | **Mean (NRx)** | -5.791667 |
| **Adjusted R-squared** | 0.732445 | **S.D. (NRx)** | 433.1299 |
| **Log likelihood** | -161.1349 | **F-statistic** | 16.74090 |
| **Durbin-Watson stat** | 2.245336 | **P-Value** | 0.000005 |

**Viagra – Alberta ARIMA (0,1,1)(0,0,1) Model**

**Dependent Variable:** Alberta NRx Volume
**Method:** Least Squares
**Sample:** 1999:07 2001:06

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | -1.349543 | 356.3068 | -0.003788 | 0.9970 |
| **C** | 1928.293 | 973.2956 | 1.981200 | 0.0622 |
| **Lagged NRx** | -0.683603 | 0.350315 | -1.951396 | 0.0659 |
| **Moving Average(1)** | 0.258483 | 0.310489 | 0.832503 | 0.4155 |
| **Seasonal MA(12)** | 0.885484 | 0.000181 | 4903.250 | 0.0000 |

| | | | |
|---|---|---|---|
| **R-squared** | 0.787229 | **Mean (NRx)** | 4.208333 |
| **Adjusted R-squared** | 0.742435 | **S.D. (NRx)** | 330.0710 |
| **Log likelihood** | -154.1567 | **F-statistic** | 17.57444 |
| **Durbin-Watson stat** | 1.972104 | **P-Value** | 0.000003 |

# APPENDIX 7

# ZYBAN INTERVENTION TIME-SERIES ANALYSIS

In order to determine the necessary level of differencing examination of the time-series plot (Figure 5), autocorrelation (AC), and partial autocorrelation (PAC) (Figure 8) was used. Based on the fact that lag 1 was within the two standard error bounds of the PAC plot 1 level of differencing was specified.

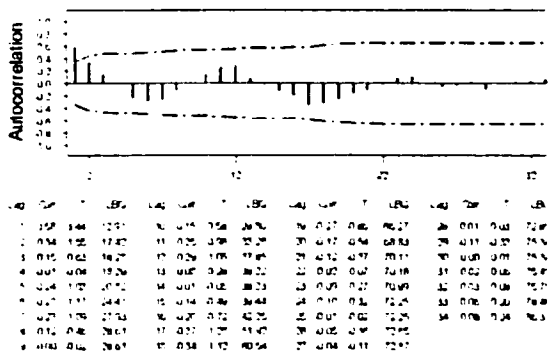
In order to determine the number of autoregressive ($p$) and moving average ($q$) parameters necessary to yield an effective model of the process several models were assessed. After considering the coefficients of determination ($R^2$), F-values, and significance levels of several alternative regression models, one with 1st level differencing (d), 1 moving average (q) parameter, 1 seasonal moving average parameter (sq), and 0 autoregressive (p) parameters was appropriate for each of the series: (p,d,q)(sp,sd,sq) = (0,1,1)(0,0,1).

NRx Volume = DTCA + C + D(NRX) + NRX(-1) + MA(1) + SMA(12)

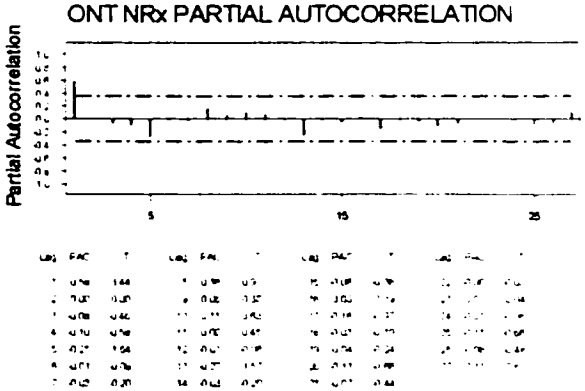
The (0,1,1)(0,0,1) model selection was justified by measuring determining that the residuals of the model were stationary and significantly different from zero using the Box-Ljung Q-statistic. Because the error series associated with the calculated ARIMA models were stationary and none of the values were significantly different from zero using the Box-Ljung Q-statistic (Table 13), and $R^2$ values were high (Tables 14-16), the ARIMA (0,1,1)(0,0,1) model was correctly specified.

# Zyban Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta

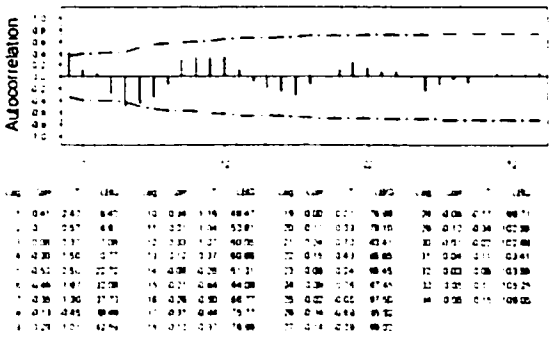
ONT NRx AUTOCORRELATION



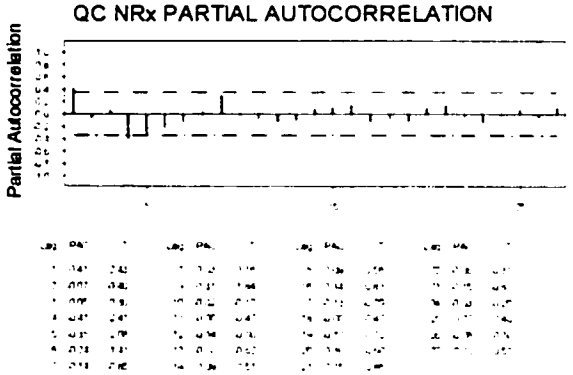

ONT NRx PARTIAL AUTOCORRELATION



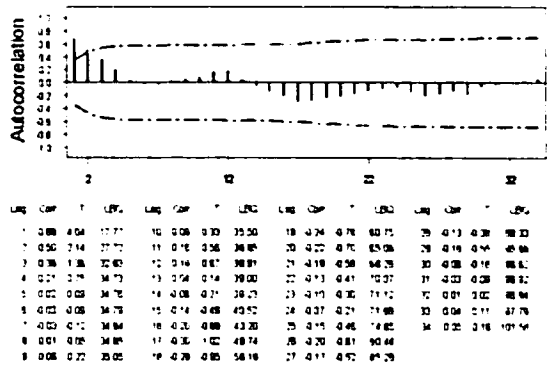

QC NRx AUTOCORRELATION



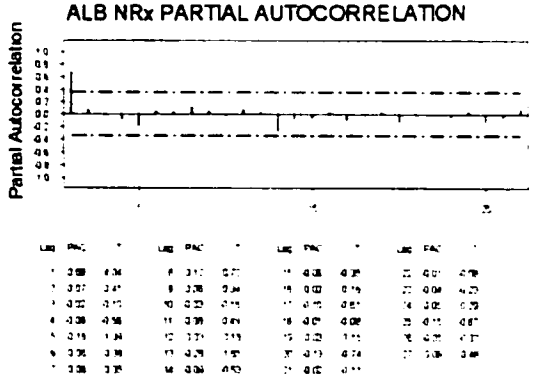

QC NRx PARTIAL AUTOCORRELATION




ALB NRx AUTOCORRELATION




ALB NRx PARTIAL AUTOCORRELATION



**Zyban Autocorrelation and Partial Autocorrelation – Ontario, Quebec, Alberta ARIMA (0,1,1)(0,0,1) Model**

| | Ontario | | | | | Quebec | | | | | Alberta | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob | | AC | PAC | Q-Stat | Prob |
| 1 | -0.024 | -0.024 | 0.0161 | | 1 | 0.024 | 0.024 | 0.0161 | | 1 | 0.039 | 0.039 | 0.0419 | |
| 2 | -0.090 | -0.090 | 0.2530 | | 2 | -0.183 | -0.184 | 1.0002 | | 2 | 0.023 | 0.022 | 0.0577 | |
| 3 | -0.023 | -0.028 | 0.2698 | 0.603 | 3 | -0.278 | -0.278 | 3.3785 | 0.066 | 3 | 0.218 | 0.216 | 1.5127 | 0.219 |
| 4 | -0.124 | -0.134 | 0.7611 | 0.683 | 4 | -0.017 | -0.055 | 3.3880 | 0.184 | 4 | 0.056 | 0.042 | 1.6145 | 0.446 |
| 5 | 0.100 | 0.090 | 1.0967 | 0.778 | 5 | 0.232 | 0.146 | 5.2092 | 0.157 | 5 | 0.159 | 0.156 | 2.4657 | 0.482 |
| 6 | -0.129 | -0.156 | 1.6922 | 0.792 | 6 | 0.052 | -0.030 | 5.3067 | 0.257 | 6 | 0.043 | -0.013 | 2.5309 | 0.639 |
| 7 | 0.110 | 0.126 | 2.1434 | 0.829 | 7 | 0.216 | 0.298 | 7.0513 | 0.217 | 7 | 0.025 | 0.004 | 2.5537 | 0.768 |
| 8 | -0.204 | -0.267 | 3.7887 | 0.705 | 8 | 0.016 | 0.162 | 7.0611 | 0.315 | 8 | 0.080 | 0.011 | 2.8064 | 0.833 |
| 9 | -0.028 | 0.039 | 3.8228 | 0.800 | 9 | -0.147 | -0.050 | 7.9733 | 0.335 | 9 | -0.143 | -0.178 | 3.6634 | 0.818 |
| 10 | -0.170 | -0.333 | 5.1180 | 0.745 | 10 | -0.217 | -0.139 | 10.086 | 0.259 | 10 | -0.193 | -0.242 | 5.3463 | 0.720 |
| 11 | 0.051 | 0.195 | 5.2444 | 0.813 | 11 | -0.058 | -0.100 | 10.246 | 0.331 | 11 | 0.013 | -0.022 | 5.3547 | 0.802 |
| 12 | 0.332 | 0.112 | 10.963 | 0.360 | 12 | 0.231 | 0.000 | 13.023 | 0.222 | 12 | 0.036 | 0.101 | 5.4214 | 0.861 |
| 13 | 0.014 | 0.194 | 10.973 | 0.446 | 13 | 0.113 | -0.035 | 13.743 | 0.248 | 13 | -0.173 | -0.092 | 7.1046 | 0.791 |
| 14 | 0.100 | -0.031 | 11.581 | 0.480 | 14 | -0.064 | -0.079 | 13.998 | 0.301 | 14 | -0.004 | 0.086 | 7.1055 | 0.851 |
| 15 | -0.114 | 0.068 | 12.466 | 0.490 | 15 | -0.221 | -0.129 | 17.308 | 0.186 | 15 | -0.145 | -0.106 | 8.5220 | 0.808 |
| 16 | 0.010 | -0.101 | 12.473 | 0.568 | 16 | 0.021 | 0.117 | 17.341 | 0.238 | 16 | -0.050 | 0.029 | 8.7111 | 0.849 |
| 17 | -0.048 | 0.007 | 12.667 | 0.628 | 17 | -0.108 | -0.177 | 18.319 | 0.246 | 17 | -0.084 | -0.097 | 9.3129 | 0.861 |
| 18 | -0.063 | -0.169 | 13.045 | 0.669 | 18 | 0.052 | 0.026 | 18.577 | 0.291 | 18 | -0.263 | -0.222 | 15.966 | 0.455 |
| 19 | 0.034 | 0.050 | 13.177 | 0.724 | 19 | -0.025 | -0.102 | 18.648 | 0.349 | 19 | 0.109 | 0.066 | 17.295 | 0.435 |
| 20 | -0.120 | -0.129 | 15.118 | 0.654 | 20 | -0.050 | -0.165 | 18.991 | 0.392 | 20 | -0.034 | -0.009 | 17.447 | 0.493 |
| 21 | -0.048 | 0.048 | 15.511 | 0.690 | 21 | -0.046 | -0.100 | 19.341 | 0.435 | 21 | -0.167 | -0.019 | 22.174 | 0.276 |
| 22 | -0.035 | 0.050 | 15.793 | 0.729 | 22 | -0.047 | 0.093 | 19.837 | 0.468 | 22 | 0.033 | 0.055 | 22.416 | 0.318 |
| 23 | -0.026 | -0.072 | 16.014 | 0.769 | 23 | -0.001 | -0.063 | 19.837 | 0.532 | 23 | -0.009 | 0.059 | 22.443 | 0.374 |

**Zvban – Ontario ARIMA (0,1,1)(0,0,1) Model**

**Dependent Variable:** Ontario NRx Volume
**Method:** Least Squares
**Sample:** 1998:09 2000:09

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 4761.514 | 261.9605 | 18.17646 | 0.0000 |
| **C** | 5827.840 | 466.1356 | 12.50246 | 0.0000 |
| **Lagged NRx** | -0.637418 | 0.036677 | -17.37905 | 0.0000 |
| **Moving Average (1)** | 0.989900 | 0.000156 | 6350.761 | 0.0000 |
| **Seasonal MA(12)** | 0.885457 | 0.124840 | 7.092725 | 0.0000 |

| | | | |
|---|---|---|---|
| **R-squared** | 0.936828 | **Mean (NRx)** | 171.1200 |
| **Adjusted R-squared** | 0.924194 | **S.D. (NRx)** | 2235.092 |
| **Log likelihood** | -193.2405 | **F-statistic** | 74.14902 |
| **Durbin-Watson stat** | 1.932840 | **P-Value** | 0.000000 |

**Zvban – Quebec ARIMA (0,1,1)(0,0,1) Model**

**Dependent Variable:** Quebec NRx Volume
**Method:** Least Squares
**Sample:** 1998:09 2000:09

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 4436.357 | 691.1291 | 6.418998 | 0.0000 |
| **C** | 4614.555 | 1013.314 | 4.553924 | 0.0002 |
| **Lagged NRx** | -0.733266 | 0.097446 | -7.524836 | 0.0000 |
| **Moving Average (1)** | 0.978806 | 0.056450 | 17.33939 | 0.0000 |
| **Seasonal MA(12)** | 0.854843 | 0.060775 | 14.06567 | 0.0000 |

| | | | |
|---|---|---|---|
| **R-squared** | 0.856153 | **Mean (NRx)** | 74.92000 |
| **Adjusted R-squared** | 0.827383 | **S.D. (NRx)** | 2364.688 |
| **Log likelihood** | -204.9357 | **F-statistic** | 29.75905 |
| **Durbin-Watson stat** | 2.002333 | **P-Value** | 0.000000 |

**Zyban – Alberta ARIMA (0,1,1)(0,0,1) Model**

**Dependent Variable:** Alberta NRx Volume
**Method:** Least Squares
**Sample:** 1998:09 2000:09

| Variable | Coefficient | Std. Error | t-Statistic | Prob. |
|---|---|---|---|---|
| **DTC** | 1807.620 | 314.9863 | 5.738728 | 0.0000 |
| **C** | 2710.394 | 405.3449 | 6.686637 | 0.0000 |
| **Lagged NRx** | -0.632662 | 0.070347 | -8.993437 | 0.0000 |
| **Moving Average (1)** | 0.647332 | 0.086785 | 7.459013 | 0.0000 |
| **Seasonal MA(12)** | 0.885340 | 0.000137 | 6451.117 | 0.0000 |

| | | | |
|---|---|---|---|
| **R-squared** | 0.894745 | **Mean (NRx)** | 27.84000 |
| **Adjusted R-squared** | 0.873694 | **S.D. (NRx)** | 1177.535 |
| **Log likelihood** | -183.6005 | **F-statistic** | 42.50374 |
| **Durbin-Watson stat** | 1.757780 | **P-Value** | 0.000000 |